2001

Perceptual learning in visual cortex : a transcranial magnetic stimulation study

Kelly Elizabeth Neary
San Jose State University

Follow this and additional works at: https://scholarworks.sjsu.edu/etd_theses

---

Recommended Citation

Neary, Kelly Elizabeth, "Perceptual learning in visual cortex : a transcranial magnetic stimulation study" (2001). *Master's Theses*. 2231.
DOI: <https://doi.org/10.31979/etd.6f93-udt2>
https://scholarworks.sjsu.edu/etd_theses/2231

This Thesis is brought to you for free and open access by the Master's Theses and Graduate Research at SJSU ScholarWorks. It has been accepted for inclusion in Master's Theses by an authorized administrator of SJSU ScholarWorks. For more information, please contact scholarworks@sjsu.edu.

INFORMATION TO USERS

This manuscript has been reproduced from the microfilm master. UMI films the text directly from the original or copy submitted. Thus, some thesis and dissertation copies are in typewriter face, while others may be from any type of computer printer.

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleedthrough, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send UMI a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

Oversize materials (e.g., maps, drawings, charts) are reproduced by sectioning the original, beginning at the upper left-hand corner and continuing from left to right in equal sections with small overlaps.

Photographs included in the original manuscript have been reproduced xerographically in this copy. Higher quality 6" x 9" black and white photographic prints are available for any photographs or illustrations appearing in this copy for an additional charge. Contact UMI directly to order.

**ProQuest Information and Learning
300 North Zeeb Road, Ann Arbor, MI 48106-1346 USA
800-521-0600**

UMI®

**PERCEPTUAL LEARNING IN VISUAL CORTEX:
A TRANSCRANIAL MAGNETIC STIMULATION STUDY**

A Thesis

Presented to

The Faculty of the Department of Biological Sciences

San Jose State University

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

By

Kelly Elizabeth Neary

December 2001

UMI Number: 1407307

UMI Microform 1407307

Copyright 2002 by ProQuest Information and Learning Company.

**All rights reserved. This microform edition is protected against
unauthorized copying under Title 17, United States Code.**

**ProQuest Information and Learning Company
300 North Zeeb Road
P.O. Box 1346
Ann Arbor, MI 48106-1346**

© 2001

Kelly Elizabeth Neary

ALL RIGHTS RESERVED

APPROVED FOR THE DEPARTMENT OF BIOLOGICAL SCIENCES

Dr. Sulekha Anand

Dr. John Hotson, Santa Clara Valley Medical Center

Dr. Michael Sneary

APPROVED FOR THE UNIVERSITY

ABSTRACT

PERCEPTUAL LEARNING IN VISUAL CORTEX: A TRANSCRANIAL MAGNETIC STIMULATION STUDY

by Kelly Elizabeth Neary

Perceptual learning may increase the strength of connections between cortical neurons. Transcranial magnetic stimulation (TMS), which transiently perturbs visual perception, was used to test whether learning a line orientation task would strengthen visual circuits. Nine subjects detected the presence of an odd element, a line which differed from distractor lines in orientation. In Experiment 1, performance on the task improved over time, demonstrating that the task was learnable. In Experiments 2 and 3, during randomly selected trials, TMS was delivered at various delays and intensities to occipital cortex. In Experiment 2, performance in TMS trials did not significantly change as subjects learned the task, suggesting that learning does not strengthen visual circuits so that they are more resistant to TMS. In Experiment 3, when feedback was given in TMS trials, performance did not change after several weeks of training, indicating that subjects cannot learn to overcome TMS.

ACKNOWLEDGMENTS

I would like to thank my graduate committee: Dr. Sulekha Anand, Dr. John Hotson and Dr. Michael Sneary. In particular I would like to express my gratitude to Dr. Anand for her tremendous help and support with conducting my research and writing my thesis and I would like to convey my appreciation to Dr. Hotson for the use of his laboratory to carry out my research, and for his insightful comments about my results. Finally, I would like to express my thanks to all those who participated in this research, including my husband Kevin.

TABLE OF CONTENTS

List of Tables	viii
List of Figures	ix
Introduction	1
Perceptual Learning	1
Transcranial Magnetic Stimulation (TMS)	16
Perceptual Learning and TMS	27
Purpose	29
General Methods	30
Experiment 1	
Purpose	33
Methods	34
Results and Discussion	35
Experiment 2	
Purpose	38
Methods	38
2.1 Methods and Results.....	45
2.2 Methods and Results.....	49
2.3 Methods and Results.....	53
Results and Discussion	54
Experiment 3	
Purpose	62

Methods	63
Results and Discussion	65
General Discussion	70
Conclusions	78
Appendix I: Human Subjects Approval	80
Literature Cited	83

LIST OF TABLES

Table 1	Summary of variables in Experiment 2.....	39
Table 2	Timeline of procedures involved in Experiment 2.....	40

LIST OF FIGURES

Figure 1	The odd element detection task	32
Figure 2	Learning curves - Experiment 1	36
Figure 3	Psychometric curves - Experiment 1	37
Figure 4	The vertical displacement task.....	41
Figure 5	The generalization task.....	44
Figure 6	Learning curves - Experiment 2.1.....	47
Figure 7	TMS sessions - Experiment 2.1.....	48
Figure 8	Learning curves - Experiment 2.2.....	51
Figure 9	TMS sessions - Experiment 2.2.....	52
Figure 10	Learning curves - Experiment 2.3.....	55
Figure 11	TMS sessions - Experiment 2.3.....	56
Figure 12	Psychometric curves - Experiment 2.....	58
Figure 13	Learning generalization curves - Experiment 2.....	59
Figure 14	TMS time window of suppression - Experiment 2.....	61
Figure 15	Learning curves - Experiment 3.....	66
Figure 16	Low intensity psychometric curves - Experiment 3.....	67
Figure 17	High intensity psychometric curves - Experiment 3.....	68

Perceptual learning, in short, is the concept that with practice perception can improve (Gibson, 1953). The term perceptual learning generalizes to learning in all of the senses; this paper is concerned with perceptual learning in vision. With practice, there is improvement in the discrimination of stimulus attributes such as color, movement, orientation, and size. This concept is the basis for perceptual learning in vision. In this study, I am investigating the neural basis of perceptual learning in vision using transcranial magnetic stimulation, a technique for non-invasively interacting with cortical neurons.

Perceptual Learning

Extensive research has been conducted on perceptual learning in the visual system. Perceptual learning of orientation has been demonstrated with line arrays (Ahissar & Hochstein, 1993; Ahissar & Hochstein, 1996; Ahissar & Hochstein, 1997; Karni & Sagi, 1991; Ramachandran & Braddick, 1973), with alternating light and dark bands of random width (Schoups, Vogels, & Orban, 1995), and with complex waveform gratings (Fiorentini & Berardi, 1980; Fiorentini & Berardi, 1981). Perceptual learning of spatial frequency discrimination has also been seen in complex waveform gratings (Fiorentini & Berardi, 1980; Fiorentini & Berardi, 1981). Perceptual learning in the discrimination of motion direction has been shown using random dot kinematograms (Ball & Sekuler, 1987; Liu, 1999; Liu & Vaina, 1998; Vaina, Sundaeswaran, & Harris, 1995). These studies have also tested whether learning is specific to the trained stimulus attribute (orientation, spatial frequency, and direction of motion) or whether it will generalize to other orientations, spatial frequencies, or directions of motion. It has also

been shown that learning is specific to retinal location of the stimulus (Ahissar & Hochstein, 1996; Ball & Sekuler, 1987; Fiorentini & Berardi, 1981; Karni & Sagi, 1991; Schoups et al., 1995; Shiu & Pashler, 1992), but that learning is not specific to the eye that has been trained to see the image (Ahissar & Hochstein, 1996; Fiorentini & Berardi, 1981; Schoups & Orban, 1996; Schoups et al., 1995; Vaina et al., 1995). The current literature on perceptual learning in vision will be reviewed.

Perceptual Learning of Different Stimulus Attributes

Orientation

In one of the first studies of perceptual learning, a group of investigators studied learning of line orientation (Karni & Sagi, 1991). The stimulus was made up of several distractor lines oriented horizontally, with a target group made up of three oblique lines, positioned adjacent to one another along either a horizontal or vertical axis. The subjects' task was to determine whether the orientation of the target group was vertical or horizontal. During different trials, the target group was located in various positions in the array. The time interval between stimulus presentation and mask presentation, called the stimulus onset asynchrony (SOA), varied between trials. The threshold SOA was determined to be the SOA which yielded a performance of 80%. Threshold SOA was determined over multiple days as subjects were trained with the task and was found to decrease over time until it leveled off. Orientation specificity was tested by rotating the target lines from the trained orientation to a new one which differed by 90°, e.g. from 135° to 45°, or from 45° to 135°, depending on which oblique target line orientation the subject was trained with. There was no significant change in performance after the target

orientation was changed, indicating that learning transferred to the new target line orientation. However, when the orientation of the distractors was changed from horizontal to vertical, while the target lines were in the trained orientation, threshold SOA increased toward its pre-training level (Karni & Sagi, 1991). In this study, the learning transferred to new target line orientations but not to new distractor orientations.

In contrast, other research was able to demonstrate that perceptual learning that was specific for target orientation. Ahissar and Hochstein (1993) studied orientation specificity with line arrays by training subjects on a pop-out detection task. The stimulus was a 7 by 7 array of oblique distractor lines oriented 30° clockwise from vertical. During half of the trials one of those lines was a target which had an orientation that was 60° clockwise from vertical. The subjects' task was to determine whether or not this "odd element" existed. Performance was assessed by determining threshold SOA. After training over several sessions, the threshold SOA decreased to a steady level. At that point, target orientation was rotated by 90°. This change in target orientation resulted in an increase in threshold SOA toward the pre-training level (Ahissar & Hochstein, 1993) indicating that learning did not transfer to the new target line orientation.

This concept of orientation specificity in line arrays was further examined in a later study by the same investigators (Ahissar & Hochstein, 1996). The stimulus in this experiment was similar to the one used in their previous study: a 7 by 7 array of lines, with distractors oriented at an angle 15° to 75° counter-clockwise from horizontal (each subject individually was trained at only one of those distractor orientations). Targets differed from distractors by a 30° clockwise rotation from the distractor position.

Training on the task led to a gradual decrease in threshold SOA. Training ended when performance reached an asymptote. In some subjects, after training, both distractors and targets were rotated by 90° from the trained position. Threshold SOA increased significantly after rotation. Similarly, when distractors and targets were rotated by 30°, threshold SOA increased. However, when distractors and targets were rotated by 15°, there was little or no effect on performance. From these results it can be concluded that learning generalizes to orientations which differ from the trained orientation by 15° to 30°. In another group of subjects, either the distractors or the targets, but not both, were rotated by 60° from the trained orientation. Threshold SOA increased when either distractors or targets were rotated, demonstrating specificity of learning for both distractor and target orientations. Interestingly, however, when performance on the mirror image of the trained stimulus was measured, there was complete transfer of learning (Ahissar & Hochstein, 1996).

Ahissar and Hochstein (1997) also found that the degree of transfer of learning to different orientations is dependent on the difficulty of the trained task. Subjects were trained on four different tasks that differed in their relative difficulty. Difficulty was measured as the angle difference between the target and distractors as well as the number of possible target locations. After training was complete, target and distractor orientations were switched, for example trained distractors were oriented 30° and targets were oriented 60° clockwise from vertical; after being switched, distractors were 60° and targets were 30°. On the two easy tasks, performance with the new distractor and target orientations was not different from the post-training performance, but on the two difficult

tasks threshold SOA increased toward pre-training performance after target and distractor positions were switched (Ahissar & Hochstein, 1997). Learning of a difficult task may therefore involve a different mechanism than learning an easy task, resulting in a more stimulus-specific type of learning than learning an easy task.

Shoups et al. (1995) used an image of alternating light and dark bands of random width to study perceptual learning of orientation. There was a reference stimulus in which the bands were oriented 45° to the left of vertical and a second stimulus in which the bands were rotated either clockwise or counterclockwise from the reference orientation. The subjects' task was to determine whether this rotation was clockwise or counterclockwise. The difference between the orientation of the reference and the second stimulus varied and the smallest difference, the just noticeable difference or JND, detected by the subjects was determined for each training day. Training led to a decrease in JND over time. After the JND leveled off for the trained orientation, the stimulus reference orientation was shifted by 90° to a new orientation which was 45° to the right of vertical, and consequently to the mirror image of the trained stimulus. JND values significantly increased, indicating that learning did not transfer to this new orientation (Schoups et al., 1995). Unlike Ahissar and Hochstein (1996) in this study learning did not generalize between mirror images. The different stimuli in the two studies could account for the discrepancy in their results.

Perceptual learning has also been demonstrated using complex waveform gratings (Fiorentini & Berardi, 1980). Subjects were presented with two different vertical gratings, gratings A and B separated by a 500 ms time interval, whose spatial phase

differed by 90°. The order of presentation of the two gratings was different from trial to trial. The subjects' task was to state whether grating A was presented first or second. Performance, measured as percentage of correct discriminations, improved over time. After performance was nearly 100%, subjects were presented with two gratings which only differed from the trained gratings in their orientation; they were horizontally, rather than vertically, oriented. Performance significantly dropped in trials with the new orientation (Fiorentini & Berardi, 1980), indicating that learning to discriminate between gratings is orientation specific.

A later study by the same investigators expanded on the findings of the previous study (Fiorentini & Berardi, 1981). Again, using vertically oriented gratings, the subjects were trained on a grating discrimination task. Similar to the previous study, subjects were presented with two gratings (A and B) which differed in spatial phase. The order of presentation of the two gratings was randomly chosen, and during each trial the subject indicated whether grating A was presented first or second. The percentage of correct discriminations increased with training. After an asymptote in performance was observed, subjects discriminated between gratings which were horizontally oriented. There was a significant decrease in performance with the novel orientation. Next, gratings were rotated 30° clockwise from the vertical, trained orientation. Performance was not significantly different at this new orientation. However, when the gratings were rotated 45° counterclockwise of the vertical gratings, there was no transfer of learning; performance was significantly lower on this new orientation. From this evidence, the authors proposed that learning generalizes to gratings which differ from the trained

orientation by up to 45°, and that above 45° the new orientation must be learned (Fiorentini & Berardi, 1981).

Spatial Frequency in Gratings

In addition to finding orientation specificity in perceptual learning, Fiorentini and Berardi (1980) tested whether perceptual learning was also specific to the spatial frequency of gratings. Spatial frequency is the frequency of oscillations between light and dark bands in a grating, measured as the number of cycles per degree. Subjects were trained on the same grating discrimination task previously discussed. The spatial frequency of both gratings was 1 cycle per degree. After performance on the task leveled off, the spatial frequency of the two gratings was changed. First, the spatial frequency was changed to 0.5 cycles per degree and performance was measured. Next, the spatial frequency was changed to 2 cycles per degree and performance was measured. With both changes in spatial frequency, performance was significantly lower with the novel spatial frequency than with the trained spatial frequency (Fiorentini & Berardi, 1980), indicating that there was no transfer of learning across the different spatial frequencies. This was one of the first studies providing evidence that perceptual learning is spatial frequency specific.

Fiorentini and Berardi followed up that study with another, similar study to further develop the concept of spatial frequency specificity in perceptual learning of gratings (Fiorentini & Berardi, 1981). Using the same task, they trained subjects with two gratings, both of which had a higher spatial frequency than in the previous experiment (Fiorentini & Berardi, 1980). Percentage of correct discriminations increased

over time (Fiorentini & Berardi, 1981). After training, the spatial frequency of the gratings was either increased or decreased. When spatial frequency was decreased from 3 to 1.5 cycles per degree there was no transfer of learning. Likewise, when spatial frequency was increased from 3 to 6 cycles per degree there was no transfer of learning. Subjects were then trained with the 6 cycles/degree gratings. After an asymptote in performance was observed, the subjects were presented with 4.5 c/deg gratings. Performance at this new spatial frequency was not significantly different than at the 6 cycles/degree spatial frequency. The investigators concluded from these data, as well as the data obtained from their previous study, that when spatial frequency is doubled or halved learning does not transfer. When smaller changes are made to spatial frequency, however, learning does generalize (Fiorentini & Berardi, 1981).

Direction of Motion

Ball and Sekuler (1987) conducted a series of perceptual learning experiments involving coherently moving dots. In these experiments, specificity for the direction of movement of the dots was tested by training subjects on a direction discrimination task. This task involved two different intervals of motion: a reference interval and a comparison interval. The direction of movement of the two intervals could either be the same or could differ by 3° . The subject was asked to state if the movement directions were the same or were different. Performance on this discrimination task rose throughout training. After performance leveled off, the researchers changed the general direction of movement of the reference and comparison intervals. When the new direction differed from the trained direction by up to $\pm 45^\circ$, learning transferred; i.e. performance remained

the same. However, beyond those limits performance was greatly affected, particularly at directions which were directly opposite of the trained direction (Ball & Sekuler, 1987). This paper provided the first evidence of selectivity in learning of motion discrimination.

Specificity for direction of movement in perceptual learning was also observed in a later study which used a similar stimulus as the previous study (Vaina et al., 1995). Subjects were trained to discriminate between two different directions of movement of dots (right or left). The percentage of correct discriminations was determined over training days. When performance was nearly perfect, the subjects were then asked to discriminate between dots moving up and down. The percentage of correct discriminations of the new directions dropped to chance (Vaina et al., 1995), thereby lending further support to the concept that learning is specific to direction of motion.

Another study employed a novel technique to test for motion direction specificity in perceptual learning (Liu & Vaina, 1998). In this study the subjects were trained on two different pairs of random dot displays. Each pair consisted of two intervals of random dot movement. One was a reference interval and the other was a comparison interval which had a direction of movement that was either the same as the reference interval or that differed by 30°. The subjects' task was to state if the directions of the intervals were the same or different. In pair 1, dots in the reference interval were moving in a direction of 135° and the comparison interval was either 135° or 165°. In pair 2, dots in the reference interval were moving in a direction of 315° and the comparison interval was either 315° or 345°. Within each training day, the sequence of blocks was as follows: pair 1, pair 1, pair 2. The researchers proposed that if learning were specific to

direction then the two pairs would be learned independently of one another. In contrast, if learning were not direction specific then performance on pair 2 would improve faster than pair 1 since it was last in the order of training. Interestingly they found that pair 2 was learned faster than pair 1, thereby indicating that the learning transferred between the two directions. Clearly, this study disagrees with evidence from other experiments which showed that learning did not transfer between different directions. However, this difference may be due to the fact that the task in this experiment was easier than in the other two experiments because subjects discriminated between two intervals of motion which differed by a larger angle than in the other experiments.

Liu (1999) used this same approach (training on two opposing pairs of directions simultaneously) to elucidate whether the difference in results between the previous studies was due to the level of difficulty of the experiments. The task in this experiment was the same as the previous study, except that it involved discriminating between motions which differed by only 3° rather than 30° , thereby making it harder than the previous study. With the more difficult task, learning of the two pairs was independent of one another, i.e. performance on pair 2 did not improve any faster than performance on pair 1, indicating that the learning was specific to the direction of motion (Liu, 1999). Therefore, specificity of learning motion direction is dependent on relative task difficulty.

Specificity of Learning to Retinal Location

Shiu and Pashler (1992) performed an experiment which tested whether learning effects generalize to visual field locations which are different from the trained visual field location. Subjects were trained on a line orientation task which involved discrimination

between two different oblique line orientations that differed from one another by only 2.8°. Fixation was maintained in the middle of the stimulus display while the stimulus was presented in one quadrant of the display. The percentage of correct discriminations increased over time on the task. After an asymptote in performance was observed on the discrimination task, the stimulus was then presented in different quadrants of the visual field, while the subjects fixated on the middle of the display. Percentage of correct discriminations decreased significantly at the new visual field positions (Shiu & Pashler, 1992), indicating that improvement in performance does not transfer to untrained visual field locations. This article provides evidence for the specificity of learning to the retinal location of the stimulus.

Shiu and Pashler's (1992) findings have been corroborated by several experiments which have demonstrated that learning does not transfer across the visual hemifields. Fiorentini and Berardi (1981) showed that learning on their grating discrimination task did not transfer between the upper and lower half of the visual field. Additional research has shown that learning does not generalize between the right and left hemifields (Ahissar & Hochstein, 1996; Ball & Sekuler, 1987; Karni & Sagi, 1991; Schoups et al., 1995). Furthermore, like Shiu and Pashler (1992), many experiments have also provided evidence that learning does not transfer between quadrants of the same hemifield (Karni & Sagi, 1991; Schoups et al., 1995)

Interocular Transfer of Learning

There has been copious research on whether improvement in the discrimination of visual stimulus attributes presented in one eye transfers to the untrained eye. Because of

the variability between results from different experiments, it cannot be concluded definitely that there is interocular transfer of learning. However, the majority of research has been able to provide evidence to support this theory.

Several studies have demonstrated interocular transfer on orientation discrimination tasks. Fiorentini and Berardi (1981) saw complete transfer of learning between trained and untrained eyes in their grating discrimination task. Percentage of correct discriminations between two gratings, which differed in spatial phase, did not change when viewed with the untrained eye. Schoups et al. (1995) demonstrated transfer of learning between eyes on an orientation discrimination task using light and dark bands of random width oriented obliquely. JND was not significantly altered when the stimulus was viewed through the untrained eye. Ahissar and Hochstein (1996) also observed transfer between eyes on a pop-out detection task using an array of lines. Threshold SOA did not significantly change when the stimulus was presented in the opposite eye (Ahissar & Hochstein, 1996).

Karni and Sagi (1991), on the other hand, found that when subjects were trained in a line array task with one eye, learning did not transfer at all to the untrained eye. The threshold SOA was higher with the untrained eye than with the trained eye (Karni & Sagi, 1991). Schoups and Orban (1996) followed that study with a similar one using the same stimulus (horizontal background lines and oblique target lines) as well as another stimulus (oblique background and target lines). However, they were able to demonstrate complete transfer of learning between trained and untrained eyes on both the Karni and Sagi (1991) stimulus and their own stimulus (Schoups & Orban, 1996). The reason for

this discrepancy in their results is not understood, given that the tasks were identical.

Studies involving motion discrimination have also addressed interocular transfer of learning. Vaina et al. (1995) saw complete transfer of learning between eyes in a motion direction discrimination task. Percent correct was not significantly different between the trained eye and the untrained eye. In contrast, Ball and Sekuler (1987) showed incomplete transfer between trained and untrained eyes. They found that in a motion direction discrimination task, there was a 74% transfer of learning between eyes (Ball & Sekuler, 1987). They calculated the amount of transfer by dividing performance with the untrained eye by the performance with the trained eye. While the majority of learning transferred, still a significant amount did not and this fact cannot be dismissed. The difference between the results of the two studies may be explained by relative difficulty levels of the task. The study conducted by Vaina et al. (1995) was much easier than that of Ball and Sekuler (1987), as the former involved discrimination between directions which differed by 180° while the latter involved discrimination between directions which differed by 3°.

Neural mechanisms of perceptual learning

The brain location where learning-induced neural changes take place has yet to be determined. It has been hypothesized that learning takes place in visual area V1 (Karni & Sagi, 1991; Schoups & Orban, 1996; Schoups et al., 1995). This hypothesis is based on two principles. First, the specificity of learning to stimulus attributes is consistent with research which demonstrates neurons in monkey striate cortex which respond specifically to such stimulus attributes as orientation, and retinal position (Hubel & Weisel, 1968).

Second, interocular transfer of learning has been demonstrated (Ahissar & Hochstein, 1996; Fiorentini & Berardi, 1981; Schoups & Orban, 1996; Schoups et al., 1995; Vaina et al., 1995), and binocular cells have been located in monkey V1 (Hubel & Weisel, 1968). Recent research on humans using positron emission tomography (PET) also found that training on orientation discrimination tasks changes neural activity in occipital cortex (Schiltz et al., 1999), which provides further evidence that the neural location of learning is in or around area V1. Alternatively, Ahissar and Hochstein (1996) hypothesize that learning takes place later than V1 yet still early in the visual pathway, perhaps in visual areas V2 or V4. They base this hypothesis on their finding that learning sometimes did generalize between different orientations, e.g. the learning effect transferred between mirror image line orientations, or to the opposite retinal hemifield. This generalization demonstrates that learning takes place in a brain region which does not respond specifically to stimulus attributes, and therefore learning must take place later than V1. More research needs to be done to clarify exactly what brain areas change with perceptual learning.

The mechanism behind the neural changes associated with perceptual learning in visual tasks is yet unknown. However, numerous psychophysical studies have proposed a theoretical basis for learning involving connections between different neurons. One possible mechanism of learning is that neuronal circuits which are specific to the learned stimulus attribute (orientation, spatial frequency, motion) are strengthened by learning (Karni & Sagi, 1991; Polat & Sagi, 1994). Another hypothesis is that there are inhibitory lateral connections between the background of an image and the foreground (Karni &

Sagi, 1991). Therefore, after training the background “noise” is reduced so that the target signal in the foreground can be amplified.

A recent psychophysical study found supportive evidence for both hypotheses. In an experiment with Gabor signals, Doshier and Lu (1998) hypothesized that learning involves reducing both external and internal noise. Subjects were trained to discriminate between Gabor signals which were oriented obliquely either to the right or the left. The contrast between the background of the display and the Gabor signals varied. There were also eight different levels of external noise as created by increasing the density of randomly located pixels. Before training, subjects could detect the orientation of the low contrast Gabor signals with a low level of external noise. Likewise, when presented with high external noise, the stimulus contrast needed to be high in order for the subject to be able to discriminate orientation. After training, improvement in performance was seen at both the high and the low noise conditions; orientation was correctly discriminated at lower signal contrasts than prior to training. Doshier and Lu (1998) propose, therefore, that improvement in discrimination of Gabor signals with high external noise is due to a reduction in external noise signals, and improvement in discrimination of Gabor signals with low external noise is due to an enhancement in the perception of the signal. They suggest that channels within the visual system are being re-weighted so that those which are appropriate to the visual stimulus are being strengthened while those responding to the noise are being inhibited (Doshier & Lu, 1998). While this experiment provides a model to explain what neural changes are accompanied with perceptual learning, there have been no neurophysiological studies to provide direct evidence and therefore more

research needs to be done.

One method of testing the hypothesis that learning strengthens cortical circuits is to use a technique called transcranial magnetic stimulation (TMS), which can perturb human visual circuits. If these visual circuits are strengthened by perceptual learning, then they may become more resistant to the effects of TMS.

Transcranial Magnetic Stimulation

Transcranial magnetic stimulation (TMS) is a non-invasive, painless procedure which comes with very little risk of injury to the subject. It involves a stimulator that supplies an electrical current to a coil of wire and in doing so generates a magnetic field under the coil (Hallett, 2000; Jahanshahi & Rothwell, 2000). TMS works through a law of physics known as Faraday's induction (Pascual-Leone, Bartres-Faz, & Keenan, 1999), whereby the magnetic field applied to the scalp by the coil crosses through tissues like skin, muscle and bone and generates an electric field in underlying neurons which lasts around 800 μ s (Beckers & Homberg, 1991). The coil can thus be placed on various body parts in order to stimulate the neurons located there. The electrical field generated can be excitatory, causing movement when stimulating motor neurons (Barker, Freeston, Jalinous, Merton, & Morton, 1985; Barker, Freeston, Jalinous, & Jarratt, 1987), or causing phosphenes (flashes of light) when stimulating occipital cortex (Barker et al., 1985; Marg & Rudiak, 1994). Alternatively, this stimulation can have inhibitory effects, thought to be caused by the secretion of γ -aminobutyric acid (GABA), an inhibitory neurotransmitter, from the stimulated neurons (Ziemann, Lonnecker, Steinhoff, & Paulus, 1996). Therefore, when TMS is applied to the brain, the underlying region can be

transiently suppressed.

There are two types of transcranial magnetic stimulation which are used in experiments involving the human brain: rapid rate TMS (rTMS) and single pulse TMS. rTMS, in which multiple TMS pulses are fired at a particular frequency, is being explored for possible therapeutic effects. Recently, experiments have been conducted to test its efficacy in relieving the symptoms of Parkinson's disease (Pascual-Leone, Valls-Sole, Brasil-Neto, Cohen, & Hallett, 1994), in treating clinical depression (George et al., 1995; Pascual-Leone, Rubio, Pallardo, & Catala, 1996), and in treating post-traumatic stress disorder (McCann et al., 1998). Single pulse TMS is primarily used in neurological diagnoses and studies of brain functions. It was first used to diagnose neurological disorders by stimulating motor cortex and observing nerve impulse conduction time (Barker et al., 1987), and since then has become one of the latest tools in studying brain function. The current literature in which TMS is used to study visual perception will be reviewed.

Effects of TMS on Visual Perception

By interacting with different regions of the brain, TMS can be used to map the brain's functional anatomy and can provide information about the timing of brain activity. Its effect on the different cortical locations responsible for visual perception has been well documented. Research that has been conducted using single pulse TMS to study visual perception will be reviewed.

Occipital Cortex

Amassian et al. (1989) performed one of the first experiments demonstrating

suppression of visual perception by transcranial magnetic stimulation. Subjects performed a letter identification task. During half of the trials, the subjects' occipital cortex was stimulated with a round coil at 90-100% intensity. The coil was placed in the middle of the posterior side of the scalp, two centimeters above the inion (over occipital cortex). In the first part of the experiment, the time between stimulus offset and TMS stimulation (the delay) varied between 0 and 200 ms. Performance was significantly lower in trials where TMS was delivered at delays ranging from 80 to 100 ms than on trials without TMS, while performance at other delays was not significantly lowered. Since TMS decreased the ability to identify letters, striate cortex must be involved in this task. Furthermore, the timing of visual suppression indicates that visual signals arrive at striate cortex 80 to 100 ms after presentation to the retina. In a second experiment, coil location was changed. Visual suppression depended on where the coil was located on the scalp. For example, when the coil was placed to the left of the mid-line, letters presented in the right visual field were incorrectly identified while those on the left were correctly identified. Also, placing the coil above the mid-line suppressed perception of the letters on the bottom of the visual field (Amassian et al., 1989). These results show that TMS can trace occipital cortex retinotopy.

Beckers and Homberg (1991) performed a similar experiment using the same stimulus as Amassian et al. (1989) to test what effect TMS intensity has on the magnitude or the timing of suppression. At a low intensity (50%) there was no significant suppression of perception of the letters. However, at higher intensities, suppression of perception of the letters occurred. Not only did the ability to correctly identify the letters

decrease with increasing intensities, but also the time window of suppression became longer at higher intensities. For example, at 60% intensity, suppression was observed 60 to 80 ms after stimulus onset, while at 100% the effect of TMS was observed between 40 and 140 ms after stimulus onset (Beckers & Homberg, 1991). This experiment provided evidence that higher intensities the TMS effect lasts longer.

Another group of investigators used the same letter identification task as the previous studies to demonstrate how different experimental conditions alter the TMS effect (Masur, Papke, & Oberwittler, 1993). A time period of suppression similar to that found in the previous research was observed that ranged from 60 to 100 ms after stimulus onset. The researchers also demonstrated that the suppression depended on many variables. First, timing of suppression depended on TMS intensity. When TMS intensity was reduced from 100% to 90%, the most robust TMS effect was shifted from a time delay of 60 ms to a delay of 86 ms. Second, timing depended on the brightness of the stimulus. When the brightness of the white letters against the dark background was decreased, the most significant TMS effect was shifted from a time delay of 69 ms to a delay of 94 ms. This shift in delay was attributed to faster synaptic transmission at high luminances. Finally, performance depended on stimulus duration. Increasing the duration of the stimulus still resulted in an observable TMS effect, but this effect was much smaller than at shorter stimulus durations with the same TMS intensity and delay. This result may be due to the fact that a longer stimulus duration may lead to neural activity in a larger cortical area thereby requiring a higher TMS intensity to suppress the perception of the stimulus. This article demonstrates well that TMS can have very

different effects depending on the experimental conditions, and therefore those conditions should be controlled in order to accurately compare results between subjects.

A study involving number identification was conducted to test what effect stimulus luminance has on the timing of TMS suppression (Miller, Fendrich, Eliassen, Demirel, & Gazzaniga, 1996). The luminance of white numbers on a black background was varied. The delay at which TMS was applied to occipital cortex varied between 80 and 140 ms after stimulus onset. At the highest luminance, suppression was observed at a delay of 100 ms, while at the lowest luminance suppression was observed at 125 ms. These results indicate that high luminance stimuli are processed by occipital cortex faster than low luminance stimuli. This research agrees with a previous study (Masur et al., 1993) which demonstrated that the brighter the stimulus, the earlier the timing of suppression, and confirms that stimulus luminance can have an important effect on the precise timing of suppression by TMS.

Past researchers observed a TMS time window of suppression which lasted between 60 and 140 ms after stimulus onset (Amassian et al., 1989; Beckers & Homberg, 1991; Masur et al., 1993). In a recent experiment, the investigators hypothesized that they would also find this time window as well as an earlier time period of processing in V1 (Corthout, Uttl, Cowey, & Hallett, 1999a). An early window of TMS suppression corresponds to early neuronal activity in the striate cortex, which had previously been demonstrated in microelectrode studies on the monkey (Knierim & Van Essen, 1992; Maunsell & Gibson, 1992). Subjects participated in a letter identification task at the same time as they were given TMS at time delays 100 ms before to 190 ms after stimulus

presentation. When TMS was delivered from 10 ms before to 10 ms after stimulus presentation, performance was significantly lowered. A later period of TMS suppression from 90 to 100 ms was also observed, which was similar to the timing found in those previous experiments. This research provided evidence that there are two essential periods of processing in V1: one early and one late (Corthout et al., 1999a). In a subsequent experiment, two periods of suppression of activity were also observed: an early period from 20 to 60 ms after stimulus presentation and a late period from 100 to 140 ms after stimulus presentation (Corthout, Uttl, Walsh, Hallett, & Cowey, 1999b). The authors suggest that the early time period of suppression relates to the timing of information arriving at V1, and the late period relates to the timing of information leaving V1 for other visual areas.

V5 and Temporal-Parietal-Occipital Cortex

TMS over the temporal-parietal-occipital (TPO) junction has been shown to affect motion perception (Hotson, Braun, Herzberg, & Boman, 1994). TPO contains visual area V5, a motion sensitive area. The stimulus in this experiment consisted of random dots, some of which moved coherently. The subjects' task was to discriminate between four directions: up, down, right and left. The delay at which TMS was delivered over left TPO at 80% intensity varied from 50 to 250 ms after stimulus onset. Motion direction discrimination was significantly reduced by TMS during a time window of 100 to 150 ms. Furthermore, this degradation in motion perception was observed when the same stimulus was presented in the different hemifields; however, it was more significant when presented in the hemifield which was contralateral to the stimulated cerebral hemisphere

at the 100 ms delay (Hotson et al., 1994). This research suggests the possible importance of TPO in motion perception, and the timing of activity in TPO. Interestingly, the timing of activity in TPO for motion tasks overlaps with the timing of activity in occipital cortex found by the previously reported studies. One explanation for this finding is that while some motion signals have left V1 and have arrived at V5, other signals are being processed by V1. Another possible explanation is that after signals arrive at V5, they are then sent back to V1.

Beckers and Homberg (1992) used a similar random dot motion stimulus to compare the effects of stimulating V1 and V5 with TMS on motion perception. In this case, subjects discriminated between dots moving coherently to either the right or the left. The delay at which TMS was applied to occipital cortex varied between 0 to 160 ms after stimulus onset. The motion stimulus was presented in the middle of the visual field during occipital stimulation trials. TMS over occipital cortex affected motion perception significantly during a time period of 70 to 80 ms after stimulus onset (Beckers & Homberg, 1992). Next, the delay at which TMS was applied to V5 varied between 60 ms before to 160 ms after stimulus onset in increments of 20 ms. During the V5 stimulation trials, the motion stimulus was presented in visual field which was either ipsilateral or contralateral to the stimulated hemisphere. Motion perception was significantly impaired at delays of 0 to 30 ms when the stimulus was presented in the contralateral hemifield (Beckers & Homberg, 1992). Performance on the stimulus presented in the ipsilateral hemifield was unaffected by the TMS, indicating that only visual signals from the contralateral visual field are processed by V5. Based on their finding that suppression of

V5 occurred at least 40 ms earlier than suppression of V1, the authors propose that motion signals leave V5 and are sent back to V1 at a later time, and that those signals are necessary for motion perception. Unlike Hotson et al. (1994) and Anand et al. (1998), a late time window of TMS-induced suppression was not seen. The difference between the results of these two studies could be due to the large difference in the stimulus durations used by the two studies. In the study by Hotson et al. (1994) stimulus duration was 50 ms, while in the study by Beckers and Homberg (1992) stimulus duration was 140 ms. It has previously been shown that stimulus duration can have a great influence on TMS effect (Masur et al., 1993).

Another study compared the effects of suppression of V1 versus the suppression of V5 on a motion task and a letter orientation task in order to determine whether V5 selectively processes motion tasks (Beckers & Zeki, 1995). The motion task was similar to the one used in the previous experiment (Beckers & Homberg, 1992) in which subjects detected motion either to the right or to the left. TMS was delivered either to V1 or V5 at delays ranging from 60 ms before to 100 ms after stimulus onset in 10 ms increments. Stimulation of V5 degraded motion direction discrimination to chance when applied during a time window of 10 ms before to 10 ms after presentation of the stimulus, which overlaps with the time window of 0 to 30 ms found in a previous study (Beckers & Homberg, 1992). When V1 was stimulated, however, there was no significant effect of TMS on perception of motion, indicating that V1 is not involved in processing motion signals. The authors propose that some motion signals go directly to V5, rather than going through V1 first, and that these signals provide enough stimulation for motion

perception. The letter orientation task involved determining whether the gap in the letter “C” was facing towards the right or the left. With the letter task, TMS was delivered to either V1 or V5 at delays ranging from 0 to 100 ms. V1 stimulation significantly affected performance at the 80 ms delay. Performance at all other delays was not significantly degraded. Stimulation of V5 at all delays, on the other hand, did not significantly affect performance on the letter identification task (Beckers & Zeki, 1995), indicating that V5 is not involved in the perception of letters. This research suggests the functional differences between the two brain regions: V5 is more critically involved in motion perception than V1, and V1 is more critically involved in form discrimination than V5.

An experiment was conducted in which TMS stimulated TPO in order to see if there was a selective suppression of motion rather than chromatic perception (Anand, Olson, & Hotson, 1998). Also, the timing of suppression of TPO was compared to the timing of suppression of occipital cortex. The first part of the experiment compared the TMS effect on a motion defined form task to the effect on a color defined form task. The motion defined form (MDF) consisted of a display of dots, some of which moved coherently thereby creating the image of the letter “C”. The subjects’ task was to state the position of the gap of the letter (up, down, right or left). The delays at which TMS was delivered to either TPO or occipital cortex varied from 60 to 240 ms after stimulus onset. The percentage of correct identifications of gap position was significantly reduced when TMS was delivered to either TPO or occipital cortex. However, the time window of suppression by stimulation of TPO was 20-40 ms later than occipital cortex. Next, in the color defined form (CDF) task, green dots formed the letter “C”, while the remainder

of the dots were red. Again, subjects discriminated gap location. TMS was only delivered over TPO; however, the delays were the same as with the MDF task. TMS over TPO significantly affected accuracy on the CDF task; although the TMS effect was smaller for the CDF task than for the MDF task. A clear distinct effect on motion perception by TMS over TPO was therefore not seen. In the second part of the experiment, motion direction discrimination was compared to color discrimination when TMS was delivered over TPO. The motion discrimination stimulus was made up of four squares. In three of the squares dots were coherently moving in the same direction. In the fourth square, dots were moving in the opposite direction. The subject was asked to state in which square the direction of movement was opposite. In the color discrimination task, three squares were yellow while the fourth square was either green or red. The subject stated which square was a different color. TMS was delivered to TPO at delays ranging from 60 to 240 ms after stimulus onset. A TMS effect was observed with both the motion and color discrimination tasks, although TMS had a more robust effect on the motion tasks. Both parts of the experiment showed that both motion and color perception are both affected by this stimulation. However, in both experiments, the TMS effect was greater for the motion dependent tasks than for the color dependent tasks. These results may indicate that the TMS delivered over TPO was primarily stimulating a motion sensitive area, but TMS was also stimulating other areas not involved in motion perception.

A study involving stimulation of V5 demonstrated the importance of that brain region in visual search tasks (Walsh, Ellison, Battelli, & Cowey, 1998b). In this

experiment, six different search tasks were used. Some were motion-dependent, for example identifying a moving target among an array of stationary distractors, or identifying a moving target among moving and stationary distractors. Some were motion-independent, for example identifying a stationary target among stationary distractors. Reaction time was measured during trials with and without TMS. TMS was delivered to V5 at the following delays: 0, 50, 100, 150, 200 and 250 ms. The TMS effect varied depending on whether motion signals were needed to identify the target. With the motion-dependent tasks, TMS significantly increased reaction time at most delays. With the motion-independent tasks, TMS did not increase reaction time, and in fact sometimes even decreased reaction time (Walsh et al., 1998b). From these results, the authors propose that V5 is not only involved in motion perception, but it is also involved in providing attention to motion dependent stimuli which is necessary for visual search tasks. The validity of their conclusions is not known, given that the investigators observed reaction time. Since reaction time does not measure performance accuracy, it is unclear what a decrease in reaction time with learning indicates. The subjects could be performing the task faster while sacrificing accuracy.

Parietal Cortex

Research investigating the effect of TMS on search tasks also points to the function of the parietal cortex in attention (Ashbridge, Walsh, & Cowey, 1997). In this experiment, the investigators compared the TMS effect on two different tasks. The first was a serial search task during which all distractors in an array needed to be scanned sequentially for the subject to locate a target. The second was a parallel search task

during which all elements in the array are processed at the same time resulting in the target “popping out”. Both tasks were made up of an array of 8 x 6 bars which, during half of the trials, contained a target bar. The subjects’ task was to state whether or not the target was present. In the serial search task, the target bar was green and vertically oriented and the distractor bars were green and horizontal or blue and vertical. In the parallel search task the target again was a green vertical bar and the distractors were green horizontal bars. Stimulation of right parietal cortex by TMS lowered reaction time on the serial visual search task at delays of 100 to 160 ms after stimulus onset, while reaction time on the parallel search task was not significantly affected (Ashbridge et al., 1997). These results indicate the importance of the parietal cortex during a serial, rather than parallel, search task. It is thought that serial search tasks require more attention than parallel search tasks, and therefore like V5, the parietal cortex is involved in attention.

Perceptual Learning and Transcranial Magnetic Stimulation (TMS)

Recently, research involving both perceptual learning and TMS has attempted to elucidate the neural mechanisms of perceptual learning. One study, measuring reaction time in a visual search task, involved comparing TMS effect over parietal cortex before and after training without TMS (Walsh, Ashbridge, & Cowey, 1998a). The task involved identifying a green vertical target bar among an 8 x 6 array of distractor bars which were made up of green, horizontally oriented, and blue vertically oriented bars. The subjects were instructed to indicate whether or not the target was present. At the beginning of the experiment, before training, the TMS effect on reaction time was measured. TMS was delivered over the parietal cortex, since a pilot study by the same investigators

demonstrated a robust effect of parietal cortex TMS on visual search tasks (Walsh et al., 1998a). The delays at which TMS was delivered varied from 0 to 280 ms after stimulus presentation. TMS greatly affected reaction time at delays of 100 ms to 160 ms after stimulus onset, consistent with the study by Ashbridge et al. (1997). The subjects were then trained on the search task, without TMS, until reaction time leveled off. TMS was again delivered to the subjects while they performed the search task, but no effect of TMS on reaction time was observed post-training. To see if this improvement on the task was due to a learning effect, subjects were presented with a novel search task, involving targets and distractors which were different shapes and colors. TMS over parietal cortex increased reaction time on the untrained task (Walsh et al., 1998a). The authors postulate that the parietal cortex is involved in the perception of a novel task, but that after training the parietal cortex becomes less important in the perception of the same task. However, since reaction time, rather than performance, was measured it is not known whether subjects improved in performing the search task or alternatively if they became quicker at performing the task with practice.

An absence of TMS effect on accuracy was observed after training subjects with a letter identification task (Corthout, Uttl, Walsh, Hallett, & Cowey, 2000). During every trial, TMS was applied to occipital cortex at different time delays ranging from 70 ms before to 200 ms after letter presentation. Three distinct time windows of suppression of letter perception were observed: an early window of 50 to 70 ms before stimulus presentation (termed dip 0), and two later windows of 20 to 30 ms after stimulus presentation (termed dip 1) and 80 to 120 ms after presentation (termed dip 2). The

suppression seen at dip 0 was attributed to a TMS-induced blink which interfered with perception. However, the other two dips were attributed to a disruption of the neural activity. After three weeks of testing, however, dips 1 and 2 were nearly gone. Here, again, with practice, the TMS effect was reduced; performance on the task was nearly perfect at all TMS delays. When the luminance of the stimulus was altered, thereby presenting the subject with an untrained task, dips 1 and 2 returned. The authors reason that this reduction in TMS effect is due to an increase in neuronal activity, i.e. more neurons were firing as the subjects were performing the task and therefore some of the firing cells were not suppressed by the TMS.

Purpose

Researchers have hypothesized, based on psychophysical evidence, that learning makes visual circuits stronger (Doshier & Lu, 1998; Karni & Sagi, 1991; Polat & Sagi, 1994) and that these neural changes occur in occipital cortex (Ahissar & Hochstein, 1996; Karni & Sagi, 1991; Schoups & Orban, 1996; Schoups et al., 1995). TMS, which transiently perturbs cortical neurons, may be useful in testing this hypothesis. If indeed visual circuits are strengthened by learning, then they may become less susceptible to the suppressive effects of TMS. These three experiments tested this postulate by training subjects on a line orientation discrimination task and determining the effect of TMS over occipital cortex.

General Methods

Subjects

Nine healthy, naïve subjects who were between the ages of 19 and 37 participated in this experiment. Six of the subjects were female, and three were male. All had 20/20 vision, or vision corrected with contacts, and none had any history of neurological disorder, such as brain trauma, epilepsy, uncontrolled migraines, or psychiatric disorders. Subjects were paid \$20.00 per hour for participating in the experiment. This research was conducted in Dr. John Hotson's laboratory at the California Institute for Medical Research, on the Santa Clara Valley Medical Center campus in San Jose, California. The experiments were approved by the Human Subjects-Institutional Review Board at San Jose State University as well as the Research and Human Subjects Review Committee at Santa Clara Valley Medical Center. Written informed consent was obtained from all subjects.

Apparatus

The visual displays were presented on a Macintosh G3 computer. The contrast of the computer monitor was 68%, with a 75 Hz refresh rate and a resolution of 1152 x 870. The monitor was placed 57 cm in front of the subject, whose head was stabilized with a chin and forehead rest. During sessions including transcranial magnetic stimulation (TMS), the subject wore earplugs in order to protect hearing. The experiment was run using MatLab (Ver. 5.2.1) with the Psychophysics Toolbox plug-in (Brainard, 1997).

A Cadwell MES-10 stimulator was used in this experiment to stimulate occipital cortex. This stimulator has a maximum output of 2.2 Tesla, with a 70 μ s magnetic pulse.

For stimulation of occipital cortex, the lower edge of a seven centimeter round coil was positioned one centimeter above the inion, so that the middle of the coil was centered three cm above the inion, with the handle facing up.

Stimulus

The odd element visual task used in all three experiments consisted of a 5 by 5 array of black lines in a 3° by 3° white square (Figure 1a). The stimulus was presented in the middle of a black computer screen. The subjects' task was to state whether there was a target, an odd element, among distractor lines. Distractor lines were tilted 30° to the left of vertical and target lines were rotated clockwise from the distractor orientation. The angle difference between the distractor lines and the target line, referred to as the orientation difference (OD), measured 5, 10, 15, 20, 25, 30 or 40 degrees. During trials in which the target was present, the target was randomly located in one of four locations. Figure 1b shows an example of the presence of an odd element. In this example, the odd element has an OD of 30°, as it is rotated 30° clockwise of the distractor lines so that its orientation is 0°.

The timing of a trial was as follows: a white fixation point was displayed on the middle of the black screen for 500 ms. The stimulus was then displayed for 14 ms (one frame of the monitor with a 75 Hz refresh rate), after which a black screen was displayed. The subject decided whether there was an odd element or not, entered his or her decision on the keyboard, and then pressed another key when ready for another trial. Thus, the inter-trial interval varied between subjects. There was a period of 2000 ms between the ready key and the onset of the next fixation point. During training blocks when the

Figure 1. The odd element detection task.

a. The four possible target positions are circled. During trials in which the target was present, the target appeared in one of the four positions.

b. An example of a trial in which a target is present. In this example, the odd element has an OD of 30°.

subject entered an incorrect response, an auditory tone immediately followed the subject's answer. No feedback was given when the subject was correct in training blocks. During trials with TMS, the TMS pulse was delivered at a delay which varied depending on the protocol of the experiment. The delay was measured as the time between stimulus onset and TMS pulse delivery.

Analysis

All data were analyzed with SPSS Version 10 software for Windows. A significance level of 0.05 was used for all analyses.

Experiment 1: Can the odd element detection task be learned?

Purpose

The purpose of the Experiment 1 was to determine whether naïve subjects could improve their performance on this task over time. The efficacy of this stimulus in learning studies had never been determined before. Although the stimulus used in this experiment was similar to one used by Ahissar and Hochstein (Ahissar & Hochstein, 1993; Ahissar & Hochstein, 1996; Ahissar & Hochstein, 1997), there were several differences between the two stimuli. In this study, unlike in those previous studies, the stimulus was a 5 by 5 array of lines, the possible target locations were restricted to four positions within 1° of the fixation point, and the OD of the target line varied. If this stimulus was found to be learnable, then it could be used in the other two experiments to test whether learning alters the effect of transcranial magnetic stimulation on the visual cortex. Furthermore, Experiment 1 was conducted to determine what training protocol should be used during Experiment 2.

Methods

Two subjects were tested in this experiment. To measure baseline performance on the odd element task before training, a psychometric curve was obtained for each subject. Performance was measured for seven different ODs: 5, 10, 15, 20, 25, 30, and 40 degrees. There were 70 trials with the odd element present, 10 trials per OD, and 70 trials without the odd element. The percent correct for each OD was calculated to create a psychometric curve. Three ODs were chosen for training from the psychometric curve: an easy OD (80-100% correct), a moderate OD (~50-60% correct), and a hard OD (<50% correct). For subject AG these ODs were 25, 15 and 10°. For subject DL these ODs were 30, 15, and 10°.

Once the three ODs were chosen, the subjects began training on the task. Each day consisted of nine blocks of 30 trials, 15 trials with the odd element present and 15 without. The easy OD was presented during the first block, the moderate OD during the second block, and the hard OD during the third block. This order was repeated two times so that each OD was practiced in three blocks. The percentage of correct discriminations was calculated for all nine blocks separately. Performance on the three easy OD blocks was averaged together each training day. This was repeated for the moderate and hard OD. There were one to three days in between each training session. Each training day proceeded in the same fashion until performance reached an asymptote, that is, until performance no longer improved from day to day. At that point, training was considered to be complete.

A post-training psychometric curve was obtained using the same methods used to

acquire the pre-training psychometric curve.

Results and Discussion

A two-way analysis of variance (ANOVA) with repeated measures was performed on the training data to test for main effects of time (the 10 training days) and OD (easy, moderate and hard). Performance on the task significantly improved over the 10 training sessions for all three trained ODs (Figure 2; $F(9, 9) = 3.483$, $p = 0.039$). Average percent correct increased from 86.4 to 95.0 for the easy OD, from 65.2 to 92.5 for the moderate OD and from 59.2 to 82.5 for the hard OD. For both subjects, performance leveled off after 10 days of training, a total of 900 trials for each OD.

A two-way ANOVA with repeated measures analyzed the pre-training and post-training psychometric data. It tested for main effects of time (before and after training) and OD. There was a significant difference between the pre-training and the post-training psychometric curves, indicating that the task had been learned (Figure 3; $F(1, 1) = 169.000$, $p = 0.049$). There was also a main effect of OD ($F(6, 6) = 208.077$, $p = 0.001$) and an interaction between time and OD ($F(6, 6) = 15.341$, $p = 0.002$). The interaction reflects the fact that for the 5° OD, performance dropped in both subjects from the pre-training to the post-training psychometric curve, while at all other ODs performance increased. However, this drop in performance should be interpreted with caution since performance before and after training was below chance, indicating that no learning had occurred for this most difficult OD.

The results of this experiment indicate that the odd element task was learned by AG and DL. Both subjects showed improvement on all three ODs on which they were

Figure 2. Learning curves for Experiment 1. Average performance on the trained ODs is plotted as a function of training day. Error bars indicate +1 standard deviation. Easy OD = open triangles, solid lines; moderate OD = filled squares, solid line; hard OD = open circles, dashed line.

Figure 3. Psychometric curves from Experiment 1. Performance is plotted as a function of OD. Error bars indicate ± 1 standard deviation. Pre-training curve = open circles, dashed line; post-training curve = filled circles, solid line.

trained. Thus, this odd element detection task was appropriate for a learning study and hence for use in the subsequent experiments. Like experiment 1, the first subject of the second experiment was trained on three ODs.

Experiment 2: Does perceptual learning strengthen occipital visual circuits making them more resistant to transcranial magnetic stimulation?

Purpose

There is evidence that perceptual learning may strengthen visual circuits (Doshier & Lu, 1998; Karni & Sagi, 1991; Polat & Sagi, 1994). Furthermore, research combining both perceptual learning and transcranial magnetic stimulation (TMS) has revealed that over time, training on a visual task decreases the amount of suppression by TMS (Corthout et al., 2000; Walsh et al., 1998a). The change in the magnitude of the TMS effect could be due in part to a change in the strength of neuronal connections. In this experiment, subjects were trained on the odd element detection task, and TMS effect was compared before, during and after training, to see if perceptual learning strengthens the connections between neurons in the occipital cortex. If this does occur, then those connections may become less susceptible to the effects of TMS.

Methods

There were three variables in Experiment 2: OD, TMS delay and TMS intensity. Three different protocols were run in this experiment to examine whether altering each of those variables, while keeping the others constant, affects the outcome of the experiment. In each of the three protocols, one variable had three levels while the other two variables had one (Table 1). For a step-by-step timeline of this experiment, refer to Table 2.

Table 1. Summary of variables in the three research protocols of Experiment 2.

Protocol #	Subject(s)	# ODs	# Delays	# Intensities
2.1	JV	3	1	1
2.2	DR, EL	1	3	1
2.3	CY	1	1	3

TMS Intensity and Delay

Because of differences in brain physiology or anatomy, TMS can have dissimilar effects in different subjects. A TMS intensity, measured as the percentage of maximum output of the stimulator, that is appropriate for one subject might be too high or too low for another. Using a TMS intensity that is too high, produces a ceiling effect whereby the subject has no chance of improvement in performance because the TMS essentially washes out all activity in the stimulated brain region. Using an intensity that is too low, on the other hand, would not affect activity in the stimulated brain region. Likewise, the TMS delay, measured as the amount of time in between stimulus onset and TMS pulse delivery, might be appropriate for one subject but too early or too late for another because of variability in processing time between subjects. Therefore, rather than using the same TMS intensity and delay with every subject, those parameters were determined for each individual by a process that attempted to ensure that the TMS effect was similar for all subjects.

TMS intensity and delay were determined using a vertical displacement task which was made up of two black lines, both oriented either to the left or to the right of vertical, on a white square (Figure 4). This task, rather than the odd element detection task, was used to determine these two parameters so as to avoid any learning taking place

Table 2. Timeline of procedures involved in Experiment 2.

Step	Procedure
1	Psychometric curve for the vertical displacement task
2	TMS intensity and delay determination with the vertical displacement task
3	Psychometric curve for the odd element task
4	Baseline TMS session
5	Training Day 1
6	Training Day 2
7	TMS Session 1
8	Training Day 3
9	Training Day 4
10	TMS Session 2
11	Training Day 5
12	Training Day 6
13	TMS Session 3
14	Training Day 7
15	Training Day 8
16	TMS Session 4
17	Training Day 9
18	Training Day 10
19	TMS Session 5
20	Training Day 11
21	Training Day 12
22	TMS Session 6
23	TMS time window
24	Final psychometric curve on odd element task
25	Psychometric curve on odd element task with new line orientation

Figure 4. Vertical displacement task. Two black lines were presented on a white square measuring 3° by 3° , which was displayed on a black screen. The subject indicated whether the two lines were either tilted to the left or to the right of vertical. In this example, the lines are tilted 30° to the left of vertical.

on the odd element detection task prior to the experiment. The angle from which the lines differed from vertical (0°) varied between 4° and 24° in 4° increments. The subject was asked to indicate if the lines were tilted to the left or right of vertical. A preliminary psychometric curve, without TMS, was run on six displacement angles. TMS intensity and delay were determined using the lowest angle at which performance was at 100% to ensure that the task was difficult enough for there to be an effect of TMS on performance.

TMS was delivered at various intensities and delays during multiple blocks. Each subject began at 80% intensity with delays ranging from 56 to 192 ms, in 14 ms increments, delivered in random order. There were 12 trials per delay, with control trials without TMS interwoven, and the percentage of correct discriminations was calculated for each delay. The results were plotted as a TMS time window curve. If performance was at chance (50%) at most delays, indicating that intensity was too high, intensity was reduced by 10%. If performance was above chance at most delays, indicating that intensity was too low, intensity was increased by 10%. These adjustments in intensity were made until a delay was chosen where performance was at chance, but at later or earlier delays performance was above chance. In all four subjects a delay of 112 ms was determined by this method. Subject JV was stimulated at 90% of the maximum intensity, subjects DR and EL were stimulated at 70% of the maximum, and subject CY was stimulated at 60, 55 and 50% of the maximum.

Psychometric Curves for Odd Element Task

To measure baseline performance on the odd element task, before training, a psychometric curve was obtained. Performance was measured for seven different ODs:

5, 10, 15, 20, 25, 30, and 40 degrees. There were 70 trials with the odd element present, 10 trials per OD, and 70 trials without the odd element. The percent correct for each OD was calculated to create a psychometric curve. Two days after training ended, a post-training psychometric curve was then obtained using the methods used to obtain the pre-training psychometric curve.

Psychometric Curves for Generalization Task

To test if learning generalizes to different line orientations, two days after training ended the subjects performed a generalization task which was the odd element discrimination task with novel line orientations; the distractors were oriented 55° to the right of vertical, while the odd element was rotated counterclockwise from the distractor position (Figure 5). In this task, the four possible locations of the odd element in the line array were the same as the original odd element detection task. Performance on the generalization task was measured for seven different ODs: 5, 10, 15, 20, 25, 30, and 40 degrees. There were 210 trials with the odd element present, 30 trials per OD, and 210 trials without the odd element. The percent correct for each OD was calculated to create a psychometric curve.

TMS Time Window

A post-training TMS time window of suppression was obtained from all subjects two days after training ended. The time window measured performance without feedback at various TMS delays, ranging from 56 to 196 ms for protocol 2.1 and 70 to 154 ms for protocols 2.2 and 2.3, delivered in random sequence at the intensity used during the TMS sessions. The percentage of correct discriminations was calculated at

Figure 5. Generalization task.

- a. The odd element display with the new line orientations used to test for orientation specificity of learning. The display consisted of a 5 x 5 array of black lines on a white square. Distractor lines were oriented 55° to the right of vertical. The circled lines indicate the four possible locations of the targets, lines which are rotated counterclockwise from the distractor position. During target trials, the odd element appeared in one of the four locations.
- b. An example of a trial containing a target with the odd element task with the new line orientations. In this example, the target has an OD of 30° .

each of these delays to create a time window curve.

2.1 - Methods and Results

For a step-by-step timeline of protocol 2.1, refer to Table 2. Pre-training TMS performance was obtained during a baseline TMS session. The subject was presented with the odd element detection stimulus in three blocks, one for each of the three ODs in the order of easy, moderate and finally hard OD. Each block consisted of 48 trials without feedback, 24 control and 24 TMS trials. In randomly chosen trials, TMS was delivered over occipital cortex at 90% intensity at a delay of 112 ms. Once a baseline performance with TMS was determined, training began.

The training protocol was the same as the protocol found to be effective in Experiment 1. For training, three ODs were chosen from the psychometric curve: an easy OD (80-100% correct), a moderate OD (~50-60% correct), and a hard OD (<50% correct). The ODs chosen for subject JV were 25° (easy), 15° (moderate) and 10° (hard). Training took place over 12 days. Each day consisted of nine blocks of 30 trials each, 15 trials with the odd element present and 15 without. The easy OD was presented during the first block, the moderate OD during the second, and the hard OD during the third. This order was repeated two times so that each OD was practiced in three blocks. The percentage of correct detections was calculated for all nine blocks separately. Each training day, performance in the three blocks with the same OD was averaged together. There were one to three days between every training session. After performance reached an asymptote, training was considered to be complete.

In order to assess whether there was a change in TMS performance with training,

TMS sessions were interspersed among training sessions. There were six TMS sessions, one occurring after every two training days. The TMS sessions were exactly the same as the baseline TMS session discussed above.

Subject JV showed improvement in performance on all three ODs over the 10 training days (Figure 6). Percent correct rose from the first to the last training day, from 78.3 to 100.0% for the easy OD, from 66.7 to 93.3 % for the moderate OD, and from 53.3 to 83.3% for the hard OD. However, during the TMS sessions, performance did not change from the baseline to the last TMS session (Figure 7). Performance in trials with TMS remained at chance level after training. Thus, even though learning occurred at all three ODs, the TMS effect was not reduced. One explanation for these results is that the TMS delay chosen using the vertical displacement task was inappropriate for the odd element detection task, e.g. it was too early or too late. Previous studies have shown that different tasks have discrete time windows of suppression (Amassian et al., 1989; Beckers & Homberg, 1991; Corthout et al., 1999a; Corthout et al., 1999b; Masur et al., 1993). Therefore, it is possible that the timing of TMS suppression of the vertical displacement task is different than the timing of suppression of the odd element task. To account for that possibility, in protocol 2.2 three delays were used, including the delay chosen by the vertical displacement task, plus an earlier delay and a later delay. Furthermore, subjects were trained on one OD so that they practiced with that OD in more trials than if they were trained on three ODs. By practicing more with that one OD the neural circuits may be stronger and therefore more resistant to TMS than practicing three different ODs.

Figure 6. Learning curves for subject JV in Experiment 2.1. Performance on the trained ODs is plotted as a function of training day. Easy OD = open triangles, solid line; moderate OD = filled squares, solid line; hard OD = open circles, dashed line.

Figure 7. TMS session curves for subject JV in Experiment 2.1.

a. Performance for the easy OD is plotted as a function of TMS session.

b. Performance for the moderate OD is plotted as a function of TMS session.

c. Performance for the hard OD is plotted as a function of TMS session.

TMS trials = filled circles, solid lines; control trials = open circles, dashed lines.

2.2 - Methods and Results

For a step-by-step outline of protocol 2.2, refer to Table 2. Three TMS delays were chosen for the two subjects run on this protocol, DR and EL. In addition to the 112 ms delay determined in the manner described above, (see “TMS Intensity and Delay”), an earlier delay and a later delay were also chosen, where performance was above chance (~70-75%). For subject DR, the early delay was 84 ms and the late delay was 140 ms. For subject EL, the early delay was 98 ms and the late delay was 154 ms.

Baseline TMS performance was determined in a similar manner as protocol 2.1. A total of 144 trials were run, with 24 trials at each of the three delays and 72 total control trials (without TMS), during the baseline TMS session. Percent correct was calculated at all three delays.

For training, one OD was chosen from the pre-training psychometric curve where performance was ~50-60% correct. DR was trained on a 15° OD while EL was trained on a 30° OD. Training took place over 12 days. Each training day consisted of 8 blocks of 40 trials each, 20 with the odd element present and 20 without the odd element present. Feedback was given during all training blocks. The percentage of correct discriminations from all eight blocks was averaged in order to obtain an average performance for each training day. There were one to three days in between each training day. Six TMS sessions were interspersed with the training sessions; there was one TMS session after every two training days. The TMS sessions were exactly the same as the baseline TMS session described above.

Subjects DR and EL showed improvement in performance on their trained OD

(Figure 8). The percentage of correct discriminations with this moderate OD, averaged together for both subjects, increased over the 12 training days from 81.4 to 89.7 %. The data from the TMS session were analyzed by using a two-way ANOVA with repeated measures which tested for main effects of TMS session and TMS delay. Performance in trials with TMS did not change significantly from the baseline to the last TMS session for any of the three TMS delays (Figure 9, $F(6, 6) = 2.630$, $p = 0.132$). There was no difference in performance between delays ($F(2, 2) = 1.875$, $p = 0.348$). For the early delay average performance in trials with TMS increased for both subjects from 60.9% at the baseline to 73.4% at the final TMS session. For the middle delay baseline performance increased from 59.3% to 65.6% at the final TMS session. For the late delay, performance decreased from a baseline performance of 57.8% to a final performance of 56.0%. Although the ANOVA did not find this difference significant, only two subjects were tested with this protocol and therefore power is low. So small effects may not be detectable with statistics. As shown by these data, even though learning occurred at the trained OD, only a slight difference in TMS effect at the early delay was seen. Using three different delays was not effective in finding a change in TMS effect with training. Further research needs to be done to determine whether the increase in performance on TMS trials at the early delay seen after training in both subjects is significant.

Since TMS intensity greatly alters TMS effect (Beckers & Homberg, 1991; Masur et al., 1993), a possible explanation for the results obtained in both protocols 2.1 and 2.2 is that the intensity determined by the vertical displacement task was too high for the odd element detection task. The vertical displacement tasks could be much easier

Figure 8. Learning curves for subjects DR and EL in Experiment 2.2. Average performance on the trained OD is plotted as a function of training day. Error bars indicate ± 1 standard deviation.

Figure 9. TMS session curves for Experiment 2.2.

a. Average performance in early TMS delay trials is plotted as a function of TMS session.

b. Average performance in middle TMS delay trials is plotted as a function of TMS session.

c. Average performance in late TMS delay trials is plotted as a function of TMS session.

Error bars indicate ± 1 standard deviation. With TMS = filled circles, solid lines; control = open circles, dashed lines.

than the odd element task and therefore would require a higher intensity to decrease performance to chance. To further investigate this explanation, protocol 2.3 included two more intensities which were lower than the intensity chosen by the vertical displacement task.

2.3 - Methods and Results

For a step-by-step timeline of protocol 2.3, refer to Table 2. Three TMS intensities were chosen for subject CY. The intensity and delay where performance on the vertical displacement task was at chance were determined in the manner described above (under “TMS Intensity and Delay”). The intensities 5% and 10% below this chosen intensity were also used during the experiment. For subject CY, the intensities used were 60%, 55% and 50%.

Baseline TMS performance was determined in a similar manner as protocols 2.1 and 2.2. Three blocks, one for each of the three intensities, were run. The low intensity was run first, followed by the medium intensity, and finally the high intensity. Each block consisted of 60 trials, 30 with TMS and 30 control trials. No feedback was given during these blocks.

For training, one OD was chosen from the pre-training psychometric curve where performance was ~50-60% correct. CY was trained on a 10° OD. Training sessions, which proceeded in the same manner as in protocol 2.2, took place over 12 days. There were one to two days in between each training day. Six TMS sessions were interspersed with the training sessions; there was one TMS session after every two training days. The

TMS sessions were exactly the same as the baseline TMS session described above.

Subject CY showed improvement in performance with the moderate OD over the 12 training days (Figure 10). Percent correct increased from 77.5% to 80.0% from the first training day to the last, although during training days 9 to 11 average performance was 85.9%. The dip in performance on the last day is probably due to normal variability in performance. However, it should be noted that CY was trained on an OD of 10 degrees, which is much smaller and therefore much more difficult than the ODs that the other subjects trained on. It is possible that because this OD was so difficult, CY would have never been able to detect the OD correctly 100% of the time.

Over the seven TMS sessions, improvement during trials with TMS was observed at the lowest intensity (chosen intensity minus 10%) (Figure 11) . At this intensity, performance increased from 67% to 93% from the baseline to the last TMS session. Performance with the moderate intensity (chosen intensity minus 5%) also slightly improved from 70% to 80%. Performance with the highest intensity did not improve; baseline performance was 63.3% and final performance was 70%. These results suggest that a change in TMS effect after learning can be seen at lower TMS intensities. Future studies should be conducted to test if this trend can be replicated.

Results and Discussion

Several statistical analyses were conducted on the data obtained from all four subjects averaged together. Since the protocols differed in the number of ODs, TMS delays and TMS intensities, only those variables which all four subjects had in common were used in these analyses.

Figure 10. Learning curves for subject CY in Experiment 2.3. Performance for the trained OD is plotted as a function of training day.

Figure 11. TMS session curves for subject CY in Experiment 2.3.

a. Performance is plotted as a function of low intensity TMS session.

b. Performance is plotted as a function of moderate intensity TMS session.

c. Performance is plotted as a function of high intensity TMS session.

TMS trials = filled circles, solid lines; control = open circles, dashed lines.

The percentage of correct discriminations of the moderate OD for each training day was compared with a one-way ANOVA with repeated measures, which showed a main effect of training day on performance (Figures 6, 8, 10, $F(11,33) = 4.764$, $p < 0.001$). This indicates that all four subjects improved performance with training.

A two-way ANOVA with repeated measures compared the pre- and post-training psychometric performance from the four subjects for all seven ODs. There was a significant difference between pre- and post-training psychometric data (Figure 12, $F(1,3) = 10.252$, $p = 0.049$), indicating that all subjects learned the odd element task. There was also a main effect of OD ($F(6,18) = 35.361$, $p = 0.001$), reflecting the fact that performance differs for different ODs.

To test for orientation specificity in learning, a two-way ANOVA with repeated measures compared performance on the two odd element tasks which differed in orientation to test for main effects of target orientation (trained compared to new) and the seven ODs. The analysis revealed that there was no main effect of orientation on performance (Figure 13, $F(1,3) = 8.066$, $p = 0.066$). That is, learning did transfer to the new orientation, and therefore was not orientation specific. There was a main effect of OD on performance ($F(6,18) = 24.231$, $p < 0.001$), indicating that performance depended on OD for both tasks.

Two separate one-way ANOVAs with repeated measures compared performance in the TMS sessions under the following testing conditions, which were common to all four subjects: moderate OD, 112 ms TMS delay, and highest intensity. Percent correct on trials with TMS was compared over the seven TMS sessions with a one-way ANOVA

Figure 12. Psychometric curves Experiment 2. Average performance is plotted as a function of OD. Error bars indicate ± 1 standard deviation. Pre-training curve = open circles, dashed line; post-training = filled circles, solid line.

Figure 13. Learning generalization curves for Experiment 2. Average performance is plotted as a function of OD. Error bars indicate ± 1 standard deviation. Trained orientation = filled circles, solid line; untrained orientation = open circles, dashed line.

with repeated measures, which showed no main effect of TMS session on performance (Figures 7, 9, 11, $F(6,18) = 45.394$, $p = 0.505$), indicating that subjects did not improve in TMS trials. The second analysis, comparing performance on control trials and TMS trials, showed that there was a significant effect of TMS on performance ($F(1,3) = 34.465$, $p = 0.010$). From these analyses it can be concluded that the TMS did suppress perception on the task, and that this suppression did not change significantly over the TMS sessions.

Figure 14 shows the time window of TMS suppression averaged for all four subjects. The percent correct on control trials was subtracted from the percent correct on TMS trials to obtain a value for the reduction of performance with TMS. TMS at all delays ranging from 56 to 196 ms affected performance, although performance was most notably affected during a period of 84 to 140 ms after stimulus onset.

These results indicate that although the odd element task was learned by all of the subjects, the learning did not strengthen visual circuits in the occipital cortex so that they were more resistant to TMS. An improvement in performance on TMS trials after training was observed in both subjects from protocol 2.2 at the early delay. It is possible that because sample size was small, the statistical analyses could not detect a small difference, but if sample size was increased and the same trend was observed, then this result would become statistically significant because of increased power. Also, the results of protocol 2.3 suggest that improvement in performance on TMS trials after training can be observed at lower intensities. Possible explanations for these findings will be discussed further in the General Discussion.

Figure 14. TMS time window of suppression for Experiment 2. Average reduction of performance (TMS performance minus control performance) is plotted as a function of TMS delay. Error bars indicate ± 1 standard deviation.

The learning of the task was not orientation specific. When the orientation was rotated 85° clockwise, performance did not change. This contradicts previous studies which demonstrated orientation specificity of learning in line arrays (Ahissar & Hochstein, 1993; Ahissar & Hochstein, 1996; Ahissar & Hochstein, 1997; Karni & Sagi, 1991; Ramachandran & Braddick, 1973).

Experiment 3: Can subjects learn to resist the effects of transcranial magnetic stimulation (TMS)?

Purpose

In order to test whether subjects could learn to resist the TMS effect, subjects were trained over several weeks with TMS over occipital cortex. Throughout the 16 days of training, feedback was given to subjects during TMS trials; an auditory tone indicated when the subject was incorrect. The importance of feedback has been well documented in learning studies which found that tasks could not be learned without feedback (Ball & Sekuler, 1987; Shiu & Pashler, 1992). Providing feedback in TMS trials may provide subjects with cues which will help them to develop strategies to overcome the TMS effect. Furthermore, control trials with feedback were randomly interspersed with TMS trials in hopes that the control trials would facilitate learning of the TMS trials. This approach attempted to provide the subjects with a “eureka effect”, which was previously described by Ahissar and Hochstein (1997). Their study on perceptual learning in line arrays revealed that presentation of an easy stimulus assists in the learning of a difficult stimulus (Ahissar & Hochstein, 1997). With respect to Experiment 3, the control trials were considered the easy condition and the TMS trials were considered the difficult

condition.

Methods

TMS Intensity and Delay

As previously discussed, differences in brain physiology or anatomy between subjects can alter the TMS effect. For example, a TMS intensity that is appropriate for one subject might be too high or too low for another. Therefore, rather than using the same TMS intensity for every subject, the appropriate intensity was determined for each individual by a process that attempted to ensure that the TMS effect was similar on all subjects.

A TMS delay of 112 ms was used in all three subjects of Experiment 3 since performance of all four subjects in Experiment 2 was at chance at a delay of 112 ms. TMS intensity was determined with the vertical displacement task (Figure 4) used in Experiment 2. Multiple blocks of trials were run with varying intensities to determine the lowest intensity where performance was to chance. Each subject began at 80% intensity. If performance was above chance, intensity was increased by 10% to 90%. If performance was below chance, intensity was turned down by 10% to 70%. Fine adjustments were made from there by turning the intensity up or down by 5%. The lowest intensity where performance was at chance was chosen. The intensity which was 5% below the chosen intensity was also used, since Experiment 2 showed that improvement in performance can be seen at lower TMS intensities. For subjects KH and NH intensities of 85% and 80% were used, while JS was trained with 95% and 90% intensities.

Experiment

To measure baseline performance on the odd element task, a psychometric curve was obtained for each subject before training. Performance was measured at seven different ODs: 5, 10, 15, 20, 25, 30, and 40 degrees. There were 70 trials with the odd element present, 10 trials per OD, and 70 trials without the odd element. The percent correct for each OD was calculated to create a psychometric curve. Since Experiment 3 was testing whether subjects could overcome the TMS effect by training with TMS, rather than by learning the odd element task, the OD chosen for training was one for which performance was 100%. KH and JS were trained with the 40° OD, and NH was trained with the 30° OD.

For each subject, two pre-training psychometric curves with TMS were obtained, one for each intensity, in order to see how pre-training performance for the five ODs was affected by TMS. The ODs used in the psychometric curves were 15, 20, 25, 30 and 40 degrees. For each OD there were 40 trials, 20 with TMS and 20 without. Percent correct for each of the ODs was calculated separately for the TMS trials and the control trials.

There were 16 days of training, each consisting of six blocks. For subject KH each block was 60 trials, 30 with TMS and 30 control. Due to KH's fatigue at the end of the training sessions, the number of control trials was reduced to 20 for subjects NH and JS. The number of TMS trials for those latter two subjects was the same as for KH. Of the six blocks, TMS was delivered at high intensity during three blocks and TMS was delivered at low intensity during the other three blocks. The order of the intensities was randomized so each training day had a different order. During all training sessions,

feedback was given during both TMS and control trials. Percent correct was calculated for the TMS trials and control trials separately for all six blocks. Performance in the three blocks of low intensity was then averaged together to obtain a mean performance for that intensity for the day. The same was done with the high intensity.

Two post-training psychometric curves with TMS, one for each trained intensity, were obtained in the same manner as the pre-training psychometric curves.

Results and Discussion

A three-way analysis of variance (ANOVA) with repeated measures tested for differences in performance between the 16 training days, between the two TMS intensities, and between TMS trials and control trials. There was a main effect of TMS; performance in trials with TMS was significantly lower than in control trials (Figure 15, $F(1,2) = 77.463$, $p = 0.013$). Performance in TMS trials did not change over the 16 days of training ($F(15,30) = 1.899$, $p = 0.066$). Mean performance for the low intensity began at 55.2% and ended at 56.3%. Mean performance for the high intensity began at 60.4% and ended at 55.2%. There was no significant difference in performance between the two intensities used ($F(1,2) = 4.786$, $p = 0.160$).

A three-way ANOVA with repeated measures analyzed the TMS data from the psychometric blocks to test for three main effects: time (before and after training), intensity (high and low), and OD (15, 20, 25, 30, 40). Performance in TMS trials did not differ before and after training (Figures 16a & 17a, $F(1,2) = 3.930$, $p = 0.186$). Furthermore, there was no difference in performance between the high and low intensities ($F(1,2) = 0.587$, $p = 0.524$). Finally, there was no main effect of OD

Figure 15. Learning curves for Experiment 3.

a. Average performance in the high intensity block is plotted as a function of day.

b. Average performance in the low intensity block is plotted as a function of day.

Error bars indicate ± 1 standard deviation. With TMS = filled diamonds, solid line; without TMS = open squares, dashed line.

Figure 16. Low intensity psychometric curves for Experiment 3.

a. Average performance in low intensity TMS trials is plotted as a function of OD.

b. Average performance in control trials is plotted as a function of OD.

Error bars indicate ± 1 standard deviation. Pre-training = open circles, dashed lines; post-training = filled circles, solid lines.

Figure 17. High intensity psychometric curves for Experiment 3.

a. Average performance in high intensity TMS trials is plotted as a function of OD.

b. Average performance in control trials is plotted as a function of OD.

Error bars indicate ± 1 standard deviation. Pre-training = open circles, dashed lines; post-training = filled circles, solid lines.

($F(4,8) = 1.844$, $p = 0.214$), indicating that performance with TMS did not differ between the five ODs.

A two-way ANOVA with repeated measures was performed on the control trials for the psychometric curves to test for two main effects: time and OD. There was no main effect of time on performance (Figures 16b & 17b, $F(1,2) = 14.606$, $p = 0.062$), indicating that no learning occurred in the control trials. This is likely due to the fact that performance for the trained OD was at 100% even before training began and therefore subjects were not learning to discriminate that OD. There was a main effect of OD, however ($F(4,8) = 12.345$, $p = 0.002$), indicating that performance varied on control trials, based on what OD was being presented.

These results indicate that the three subjects did not overcome the effect of TMS when trained on TMS trials. Providing feedback did not “train” visual circuits to overcome the suppressive effects of TMS.

General Discussion

Perceptual Learning

Similar to the findings of previous studies (Ahissar & Hochstein, 1993; Ahissar & Hochstein, 1996; Ahissar & Hochstein, 1997; Ahissar, Laiwand, Kozminsky, & Hochstein, 1998), this study demonstrates that training on an odd element detection task consisting of oblique target and distractor lines leads to improvement in performance. Furthermore, Experiments 1 and 2 (protocol 2.1) show that training on three levels of difficulty simultaneously leads to improvement on all three levels. During training sessions, the order of training blocks was as follows: easy OD, moderate OD, hard OD. This order of presentation may have actually facilitated learning. It has been shown previously that presentation of an easy stimulus will help learning of a hard stimulus (Ahissar & Hochstein, 1997). In my experiment, presenting the easy OD may have provided the subjects with cues in order to help them detect the moderate and hard ODs.

The improvement in performance obtained by learning a particular line orientation generalized to other orientations. After subjects reached an asymptote in performance, the distractors were rotated clockwise by 85°, and targets were rotated counterclockwise from the distractor position. There was no difference in performance between the trained and the untrained orientations. This study therefore demonstrates that learning this task is not specific to line orientation.

The discrepancy between these results and the results obtained in other studies which demonstrated orientation specificity in learning (Ahissar & Hochstein, 1993; Ahissar & Hochstein, 1997; Karni & Sagi, 1991) may be explained by considering the

manner in which learning specificity was tested. Because targets were rotated counterclockwise from the distractor position in the generalization task, the untrained target orientation was not much different from the trained target orientation. For example, the 40° OD target had an orientation of +10° in the trained task and +15° in the generalization task. The two target orientations only differed by 5°. Ahissar and Hochstein (1996) found that learning generalizes between line orientations which differ by less than 30°. Therefore, it is possible that the two tasks were in fact not that different, allowing learning to generalize between the two tasks. If targets in this study had been rotated clockwise, then orientation specificity may have been observed.

It is not known whether subjects learned the orientation of the target and distractor lines, or whether they developed a strategy for performing the task. Developing such a strategy for performing the trained task could have helped in performing the generalization task.

The results of this study provide support to Ahissar and Hochstein's (1996 & 1997) assertion that the neural changes associated with learning take place in higher visual areas. They found that learning did generalize in certain situations but not in others. For example learning transferred with easy tasks but not difficult tasks, and learning also transferred between mirror images. If learning was specific to the trained orientation and never generalized to other orientations then clearly the physiological changes resulting from learning would occur in a brain region such as V1, where neurons selectively respond to a particular orientation. However, since generalization did occur in some situations, as observed in the studies by Ahissar and Hochstein (1996 & 1997) and

in this present study, it is likely that the cortical changes take place in higher visual areas, past V1, which receive signals from V1. Ahissar and Hochstein (1996) also suggest that attention has a role in learning, and therefore the neural changes must occur in a region which is influenced by attentional mechanisms, such as V2, V3 or V4.

TMS Effect on Line Orientation Discrimination

For the first time, this study provides a time window of TMS suppression of detection of an odd element in a line array. TMS delivered over occipital cortex hindered detection during a time window occurring 84 to 140 ms after stimulus onset. This window of suppression is consistent with previous studies on the TMS effect on occipital cortex, which found suppression in letter identification tasks to occur during a time period of 60 to 140 ms after stimulus onset (Amassian et al., 1989; Beckers & Homberg, 1991; Corthout et al., 1999a; Corthout et al., 1999b; Masur et al., 1993).

This study provided evidence for the importance of occipital cortex in orientation discrimination, since TMS over occipital cortex suppressed line orientation perception during a discrete time window. This finding agrees with other research which has demonstrated the role of occipital cortex in the perception of line orientation. Research on monkeys has led to the discovery of orientation specific columns in striate cortex (Hubel & Weisel, 1968). Another study involving monkeys found that neural activity in V1 increased when the subject was presented with an odd element detection task, similar to the one used in this study (Knierim & Van Essen, 1992). A positron emission tomography study on humans found an increase in activity in occipital cortex during an orientation discrimination task (Orban, Dupont, Vogels, Bormans, & Mortelmans, 1997).

Perceptual Learning and TMS

Even though subjects learned the odd element detection task, after 12 days of training the effect of TMS was not significantly different from the baseline TMS effect. There are several possible explanations for this finding. First, learning may not have strengthened cortical circuits. It has never been documented that learning reinforces connections within the brain, although researchers have hypothesized this to be the mechanism by which perceptual learning occurs (Karni & Sagi, 1991; Polat & Sagi, 1994). The findings of the current study do not support this hypothesis. If learning does not in fact strengthen visual circuits then there would be no change in TMS performance with training, as was seen in this experiment.

A second possible explanation is that rather than occipital cortex, neural connections may be strengthened in other brain regions with perceptual learning. In this study, TMS was delivered over occipital cortex, since previous research provided psychophysical evidence that the neural changes associated with perceptual learning occur within this brain region (Karni & Sagi, 1991; Schoups & Orban, 1996; Schoups et al., 1995). Delivery of TMS using a round coil over occipital cortex results in stimulation of striate and extrastriate areas. If the neural changes associated with perceptual learning take place in brain regions other than the areas affected by TMS, then the TMS effect would not be different after training.

A third explanation for the lack of improvement in TMS trials after training is that learning did not strengthen channels enough to be resistant to TMS because the task was too difficult. Typically, TMS does not degrade performance in tasks that are too easy

(unpublished results). Perhaps alternatively, TMS degrades performance in difficult tasks too much; therefore, the TMS effect is too great to overcome with learning. It has been previously demonstrated that task difficulty is related to the number of possible target locations (Ahissar & Hochstein, 1997). In the current study, there were four possible target locations. A future study could involve an odd element detection task with two, or possibly even one, target location. As a result, the task may be easier to learn which may in fact facilitate learning, and possibly strengthen the orientation specific visual circuits even more. It would be fascinating to see if the TMS effect could be overcome with training on a task that is less difficult than the one used in this study.

A final explanation for the results of this experiment is that if learning does indeed strengthen visual circuits, then the connections formed by perceptual learning may not be strong enough to withstand the disruption caused by the TMS. It is possible that TMS intensity was too high. The TMS effect is directly related to TMS intensity (Beckers & Homberg, 1991; Masur et al., 1993). In this present study, the subjects trained on protocols 2.1 and 2.2 were given TMS at the intensity at which performance on a vertical displacement task was degraded to chance. Those subjects did not show improvement in performance on TMS trials at that intensity. Subject CY (tested on protocol 2.3) was given TMS at that same intensity as well as at two lower intensities. At the two lower intensities, CY's performance on TMS trials did improve after training. The data from CY suggest that the intensities used with the other subjects were too high, and therefore the TMS was inhibiting those neurons at a strength which could not be overcome in spite of learning.

Alternatively, CY's improvement may have been due to his becoming more comfortable with the TMS. It should be noted that the intensities used with CY were quite lower than intensities used with other subjects. Furthermore, CY was nervous about the effect of TMS in the beginning of the study. It is possible that if TMS intensity had been determined after a longer introduction to the procedure, in order to make CY more comfortable, that the intensities used would have been closer to those used in other subjects. If that had been the case, then perhaps the improvement in performance with TMS would not have been seen.

Although improvement in performance of the odd element task at the peak TMS delay was not seen in Experiment 2.2, it should be noted that both subjects improved in performance in TMS trials at the early delay. Although this result was not statistically significant, possibly due to the fact that sample size was small, it does suggest a trend. The improvement seen in both subjects could suggest that learning does indeed strengthen visual circuits, making them more resistant to TMS. Future research could be conducted to see whether this trend is observed in more subjects.

Walsh et al. (1998) saw a decrease in the TMS effect after training subjects on visual search tasks. In their study, Walsh et al. (1998) measured reaction time and found that before training, reaction time was significantly higher on trials with TMS than on control trials. After training, reaction time on TMS trials was reduced. They postulated that the neural changes associated with perceptual learning caused their observed change in reaction time with training. However, the accuracy of the subjects' answers on TMS trials is not known. It is possible that performance on TMS trials did not change after

training on the task, but rather the subjects just shortened their reaction time. In my study, which did not measure reaction time, there was no significant change in performance accuracy on TMS trials after training on the task.

Resistance to TMS

After training for 16 days with TMS, the subjects who participated in Experiment 3 did not overcome the suppressive effects of TMS. In all of the subjects, during each training day, there was very little consistent improvement in performance from block to block, and any improvement that was seen did not carry over to the next day. There was no difference in the TMS effect between the high and low intensity. A plausible explanation for these findings is that the TMS effect was too strong to overcome. TMS can stimulate GABA-ergic interneurons which will inhibit nearby neural activity (Ziemann et al., 1996). In doing so, TMS is essentially adding noise to the visual stimulus and is thereby altering the perception of the stimulus. It is possible that no amount of learning can reduce the TMS effect.

In contrast to this study, Corthout et al. (2000) observed a decrease in TMS suppression of occipital cortex by training subjects with a letter identification task for three weeks. The difference between their results and the results of this study could relate to TMS intensity or visual task. In this study TMS intensity ranged from 80 to 95%, while Corthout et al. (2000) used intensities of 55 to 75%. It is possible that subjects in that study could overcome the suppressive effects of TMS simply because the TMS effect was not very potent to begin with, while the subjects of this study were being stimulated at an intensity which was too high to ever be able to overcome. Future research should

include training on TMS trials when TMS is delivered at lower intensities. Alternatively, the difference between Corthout et al.'s (2000) results and the results of this study could also be explained by the task used in their study. After training, the letter identification task may be perceived in brain regions which are responsible for reading, rather than form discrimination. It is also possible that after training, processing of the letters bypasses occipital cortex and instead goes directly to higher brain regions. Beckers and Zeki (1995) found evidence for direct processing in V5 using a motion direction discrimination task. If, after training, the letter identification task is indeed perceived in a brain region not located within occipital cortex then no TMS effect would be observed.

Potential Confounding Variables

TMS causes eye blinks, usually because of stimulation of sensory receptors on the scalp, which could interfere with perception of the stimulus. Interruption of perception by TMS-induced eye blinks has been shown at early TMS delays of around 50 ms before stimulus presentation (Corthout et al., 1999a; Corthout et al., 1999b). Eye blinks could not have caused the observed TMS effect in this study because TMS was delivered after the stimulus was presented. The stimulus duration was always 14 ms, and the earliest that TMS was delivered was 56 ms after stimulus onset, 42 ms after the end of the stimulus duration. Therefore, the stimulus had already been presented to the retina by the time that the TMS caused the eyes to blink. The stimulator also causes a loud clicking noise which could have startled the subjects, causing them to lose fixation on the image, or causing a interference in attentional processes. However, not only did subjects wear earplugs to protect hearing, which reduced the noise of the stimulator, but also TMS

pulses always occurred after stimulus presentation so the subject saw the stimulus before the TMS could have averted their attention. Some subjects also noted that after participating in the experiment for a short while, they became used to the sound and did not feel distracted by the TMS. Therefore, it is likely that the observed TMS effect was due to a disruption of neural activity in occipital cortex and not due to other non-disruptive TMS effects.

Conclusions

Subjects learned to detect an odd element in an array of distractors. The learning effects generalized to untrained orientations. TMS over occipital cortex disrupted performance on the odd element task during a time window of 84 to 140 ms after stimulus onset, which demonstrates the importance of occipital cortex in line orientation discrimination. Although there was a trend for improvement in performance on TMS trials at early TMS delays and low TMS intensities, training subjects on the odd element task did not consistently and significantly reduce the TMS-induced suppression of occipital cortex. These findings could indicate that perceptual learning does not strengthen visual circuits, or alternatively, that if cortical connections are enhanced, these changes do not occur within occipital cortex. Another explanation for these results is that the visual circuits did not become more resistant to TMS after training because TMS intensity was too high. Training on TMS trials by providing feedback to subjects did not change performance on TMS trials, possibly because the TMS intensities used were too high or alternatively because the TMS effects simply cannot be overcome with training. This study demonstrates that TMS is a useful tool for studying the neural basis of

perceptual learning.

Appendix I. Human Subjects Approval

San José State
UNIVERSITY

**Office of the Academic
Vice President**

**Associate Vice President
Graduate Studies and Research**

One Washington Square
San Jose, CA 95192-0025
Voice: (408) 924-2480

Fax: (408) 924-2477

E-mail: gstudres@sjcs.sjsu.edu
HTTP: www.sjsu.edu

TO: Kelly Neary
1614 Oxford St., #8
Redwood City, CA 94061

81

FROM: Nabil Ibrahim, N. Ibrahim
AVP, Graduate Studies & Research

DATE: October 23, 2000

**The Human Subjects-Institutional Review Board has approved
your request to use human subjects in the study entitled:**

**"Supranuclear Control of Eye Movement
and Visual Processing"**

This approval is contingent upon the subjects participating in your research project being appropriately protected from risk. This includes the protection of the anonymity of the subjects' identity when they participate in your research project, and with regard to any and all data that may be collected from the subjects. The approval includes continued monitoring of your research by the Board to assure that the subjects are being adequately and properly protected from such risks. If at any time a subject becomes injured or complains of injury, you must notify Nabil Ibrahim, Ph.D., immediately. Injury includes but is not limited to bodily harm, psychological trauma and release of potentially damaging personal information. This approval is in effect for one-year and data collection beyond October 23, 2001 requires an extension request.

Please also be advised that all subjects need to be fully informed and aware that their participation in your research project is voluntary, and that he or she may withdraw from the project at any time. Further, a subject's participation, refusal to participate, or withdrawal will not affect any services the subject is receiving or will receive at the institution in which the research is being conducted.

**If you have any questions, please contact me at
(408) 924-2480.**

The California State University:
Chico, Fresno, Fullerton, Hayward, Long Beach, Los Angeles, Maritime Academy,
Merced, Monterey, Northridge, Pomona, Sacramento, San Bernardino, San Diego,
San Francisco, San Jose, San Luis Obispo, Stanislaus,
San Marcos, San Bernardino, Stanislaus

San José State
UNIVERSITY

**Office of the Academic
Vice President**
Associate Vice President
Graduate Studies and Research

One Washington Square
San José, CA 95192-0025
Voice: 408-283-7500
Fax: 408-924-2477
E-mail: gstudies@wahoo.sjsu.edu
<http://www.sjsu.edu>

To: Dr. Joseph Pesek
Associate Dean
Graduate Studies & Research
San José State University
San José, CA 95192-0025

cc: Kelly Neary, Dr. Sulekha Anand

From: Eileen Fortin *Eileen Fortin*
IRB Coordinator for Human Subjects

Date: November 2, 2001

This letter acknowledges that the Human Subjects-Institutional Review Board has received a request to document a change of title for a research study by Kelly Neary, a graduate student in the Department of Biological Sciences.

The original title of this IRB-approved project was:

"Supranuclear Control of Eye Movement and Visual Processing."

Kelly Neary conducted that project in connection with a study with the same title by Dr. Sulekha Anand of the Biological Sciences Department. Each researcher has requested and received separate Human Subjects approval for these studies.

The new title for the study by Ms. Neary is:

**"The Neural Basis of Perceptual Learning:
A transcranial magnetic stimulation study."**

It has been documented to the satisfaction of the Institutional Review Board that the new title of Ms. Neary's study will more accurately reflect the nature of her research. She will use this title for a master's thesis to be submitted to Graduate Studies & Research on November 2, 2001.

This letter is intended to document the approval of Kelly Neary's project by the IRB for Human Subjects, under the original title, on October 23, 2000. If there should be any question concerning this matter, please contact me at (408) 924-2479.

The California State University:
Chancellor's Office
Bakersfield, Channel Islands, Chico,
Dominguez Hills, Fresno, Fullerton,
Hayward, Humboldt, Long Beach,
Los Angeles, Maritime Academy,
Monterey Bay, Northridge, Pomona,
Sacramento, San Bernardino, San Diego,
San Francisco, San José, San Luis Obispo,
San Marcos, Sonoma, Stanislaus

Literature Cited

Ahissar, M., & Hochstein, S. (1993). Attentional control of early perceptual learning. Proceedings of the National Academy of Science, USA, 90(12), 5718-5722.

Ahissar, M., & Hochstein, S. (1996). Learning pop-out detection: specificities to stimulus characteristics. Vision Research, 36(21), 3487-3500.

Ahissar, M., & Hochstein, S. (1997). Task difficulty and the specificity of perceptual learning. Nature, 387(6631), 401-406.

Ahissar, M., Laiwand, R., Kozminsky, G., & Hochstein, S. (1998). Learning pop-out detection: building representations for conflicting target-distractor relationships. Vision Research, 38(20), 3095-3107.

Amassian, V., Cracco, R., Maccabee, P., Cracco, J., Rudell, A., & Eberle, L. (1989). Suppression of visual perception by magnetic coil stimulation of human occipital cortex. Electroencephalography and Clinical Neurophysiology, 74(6), 458-462.

Anand, S., Olson, J., & Hotson, J. (1998). Tracing the timing of human analysis of motion and chromatic signals from occipital to temporo-parieto-occipital cortex: A transcranial magnetic stimulation study. Vision Research, 38, 2619-2627.

Ashbridge, E., Walsh, V., & Cowey, A. (1997). Temporal aspects of visual search studied by transcranial magnetic stimulation. Neuropsychologia, 35(8), 1121-1131.

Ball, K., & Sekuler, R. (1987). Direction-specific improvement in motion discrimination. Vision Research, 27(6), 953-965.

Barker, A., Freeston, I., Jalinous, R., Merton, P., & Morton, H. (1985). Magnetic stimulation of the human brain. Journal of Physiology, 369, 3P.

Barker, A., Freeston, L., Jalinous, R., & Jarratt, J. (1987). Magnetic stimulation of the human brain and peripheral nervous system: an introduction and the results of an initial clinical evaluation. Neurosurgery, 20(1), 100-109.

Beckers, G., & Homberg, V. (1991). Impairment of visual perception and visual short term memory scanning by transcranial magnetic stimulation of occipital cortex. Experimental Brain Research, 87(2), 421-432.

Beckers, G., & Homberg, V. (1992). Cerebral visual motion blindness: transitory akinetopsia induced by transcranial magnetic stimulation of human area V5. Proceedings of the Royal Society of London. Series B: Biological Sciences, 249(1325), 173-178.

Beckers, G., & Zeki, Z. (1995). The consequences of inactivating areas V1 and V5 on visual motion perception. Brain, 118(Pt. 1), 49-60.

Brainard, D. (1997). The Psychophysics Toolbox. Spatial Vision, 10, 433-436.

Corthout, E., Uttl, B., Cowey, A., & Hallett, M. (1999a). Two periods of processing in the (circum)striate visual cortex as revealed by transcranial magnetic stimulation. Neuropsychologia, 37(2), 137-145.

Corthout, E., Uttl, B., Walsh, V., Hallett, M., & Cowey, A. (1999b). Timing of activity in early visual cortex as revealed by transcranial magnetic stimulation. NeuroReport, 10(12), 2631-2634.

Corthout, E., Uttl, B., Walsh, V., Hallett, M., & Cowey, A. (2000). Plasticity revealed by transcranial magnetic stimulation of early visual cortex. NeuroReport, 11(7), 1565-1569.

Dosher, B., & Lu, Z. (1998). Perceptual learning reflects external noise filtering and internal noise reduction through channel reweighting. Proceedings of the National Academy of Science, USA, 95(23), 13988-13993.

Fiorentini, A., & Berardi, N. (1980). Perceptual learning specific for orientation and spatial frequency. Nature, 287(5777), 43-44.

Fiorentini, A., & Berardi, N. (1981). Learning in grating waveform discrimination: specificity for orientation and spatial frequency. Vision Research, 21(7), 1149-1158.

George, M., Wassermann, E., Williams, W., Callahan, A., Ketter, T., Basser, P., Hallett, M., & Post, R. (1995). Daily repetitive transcranial magnetic stimulation (rTMS) improves mood in depression. Neuroreport, 6(14), 1853-1856.

Gibson, E. (1953). Improvement in perceptual judgements as a function of controlled practice or training. Psychology Bulletin, 50, 401-431.

Hallett, M. (2000). Transcranial magnetic stimulation and the human brain. Nature, 406(6792), 147-150.

Hotson, J., Braun, D., Herzberg, W., & Boman, D. (1994). Transcranial magnetic stimulation of extrastriate cortex degrades human motion direction discrimination. Vision Research, 34(16), 2115-2123.

Hubel, H., & Weisel, T. (1968). Receptive fields and functional architecture of monkey striate cortex. Journal of Physiology, 195, 215-243.

Jahanshahi, M., & Rothwell, J. (2000). Transcranial magnetic stimulation studies of cognition: an emerging field. Experimental Brain Research, 131(1), 1-9.

Karni, A., & Sagi, D. (1991). Where practice makes perfect in texture discrimination: evidence for primary visual cortex plasticity. Proceedings of the National Academy of Science, USA, 88(11), 4966-4970.

Knierim, J., & Van Essen, D. (1992). Neuronal responses to static textures patterns in area V1 of the alert Macaque monkey. Journal of Neurophysiology, 67(4), 961-980.

Liu, Z. (1999). Perceptual learning in motion direction that generalizes across motion directions. Proceedings of the National Academy of Science, USA, 96(24), 14085-14087.

Liu, Z., & Vaina, L. (1998). Simultaneous learning of motion discrimination in two directions. Cognitive Brain Research, 6(4), 347-349.

Marg, E., & Rudiak, D. (1994). Phosphenes induced by magnetic stimulation over the occipital brain: description and probable site of stimulation. Optometry and Vision Science, 71(5), 301-311.

Masur, H., Papke, K., & Oberwittler, C. (1993). Suppression of visual perception by transcranial magnetic stimulation - experimental findings in healthy subjects and patients with optic neuritis. Electroencephalography and Clinical Neurophysiology, 86(4), 259- 267.

Maunsell, J., & Gibson, J. (1992). Visual response latencies in striate cortex of the macaque monkey. Journal of Neurophysiology, 68(4), 1332-1344.

McCann, U., Kimbrell, T., Morgan, C., Anderson, T., Geraci, M., Benson, B., Wassermann, E., Willis, M., & Post, R. (1998). Repetitive transcranial magnetic stimulation for posttraumatic stress disorder. Archives of General Psychiatry, 55(3), 276-279.

Miller, M., Fendrich, R., Eliassen, J., Demirel, S., & Gazzaniga, M. (1996). Transcranial magnetic stimulation: delays in visual suppression due to luminance changes. NeuroReport, 7(11), 1740-1744.

Orban, G., Dupont, P., Vogels, R., Bormans, G., & Mortelmans, L. (1997). Human brain activity related to orientation discrimination tasks. European Journal of Neuroscience, 9(2), 246-259.

Pascual-Leone, A., Bartres-Faz, D., & Keenan, J. (1999). Transcranial magnetic

stimulation: studying the brain-behaviour relationship by induction of 'virtual lesions'. Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 354(1387), 1229-1238.

Pascual-Leone, A., Rubio, B., Pallardo, F., & Catala, M. (1996). Rapid-rate transcranial magnetic stimulation of left dorsolateral pre-frontal cortex in drug-resistant depression. Lancet, 348(9022), 233-237.

Pascual-Leone, A., Valls-Sole, J., Brasil-Neto, J., Cohen, L., & Hallett, M. (1994). Akinesia in Parkinson's disease. I. Shortening of simple reaction time with focal, single-pulse transcranial magnetic stimulation. Neurology, 44(5), 884-891.

Polat, U., & Sagi, D. (1994). Spatial interactions in human vision: from near to far via experience-dependent cascades of connections. Proceedings of the National Academy of Science, USA, 91(4), 1206-1209.

Ramachandran, V., & Braddick, O. (1973). Orientation-specific learning in stereopsis. Perception, 2(3), 371-376.

Schiltz, C., Bodart, J., Dubois, S., Dejardin, S., Michel, C., Roucoux, A., Crommelinck, M., & Orban, G. (1999). Neuronal mechanisms of perceptual learning: changes in human brain activity with training in orientation discrimination. NeuroImage, 9(1), 46-62.

Schoups, A., & Orban, G. (1996). Interocular transfer in perceptual learning of a pop-out discrimination task. Proceedings of the National Academy of Science, USA, 93(14), 7358-7362.

Schoups, A., Vogels, R., & Orban, G. (1995). Human perceptual learning in identifying the oblique orientation: retinotopy, orientation specificity and monocularly. Journal of Physiology, 483(3), 797-810.

Shiu, L., & Pashler, H. (1992). Improvement in line orientation discrimination is retinally local but dependent on cognitive set. Perception and Psychophysics, 52(5), 582-588.

Vaina, L. M., Sundaeswaran, V., & Harris, J. G. (1995). Learning to ignore: psychophysics and computational modeling of fast learning of direction in noisy motion stimuli. Cognitive Brain Research, 2(3), 155-163.

Walsh, V., Ashbridge, E., & Cowey, A. (1998a). Cortical plasticity in perceptual learning demonstrated by transcranial magnetic stimulation. Neuropsychologia, 36(4), 363-367.

Walsh, V., Ellison, A., Battelli, L., & Cowey, A. (1998b). Task-specific impairments and enhancements induced by magnetic stimulation of human visual area V5. Proceedings of the Royal Society of London. Series B: Biological Sciences, 265(1395), 537-543.

Ziemann, U., Lonnecker, S., Steinhoff, B., & Paulus, W. (1996). Effects of antiepileptic drugs on motor cortex excitability in humans: a transcranial magnetic stimulation study. Annals of Neurology, 40(3), 367-378.